

# Department of Clinical Investigation Annual Research Progress Report



**Fiscal Year 2006**

Madigan Army Medical Center  
Tacoma, Washington



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14. ABSTRACT This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, Tacoma, WA during FY 2006. Included in the individual data summary sheets are title, investigators, objective, technical approach, and progress for FY 2006. Also included in the report are personnel rosters for the program, funding information, presentations, and publications emanating from Madigan Army Medical Center during FY 2006. 127 new protocols were approved and 103 were completed in FY 2006. 222 staff members, 79 residents/fellows and 18 non-Medical Corps trainees held approved research protocols in FY 2006. 93 manuscripts were published as well as 53 abstracts and 163 presentations.					
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**ANNUAL PROGRESS REPORT**

30 SEPTEMBER 2006

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

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**FISCAL YEAR 2006**  
**DEPARTMENT OF CLINICAL INVESTIGATION**  
**MADIGAN ARMY MEDICAL CENTER**  
**TACOMA, WASHINGTON 98431**

**Introduction**

In conducting the research described in this report, the investigators adhered to the “Guide for the Care and Use of Laboratory Animals” as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9, Subchapter A, Parts I, II, and III of the Code of Federal Regulations. The investigators adhered to Title 21, Part 50 of the Code of Federal Regulations and the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

**Acknowledgments**

The DCI staff would like to acknowledge the significant and varied contributions of many individuals and organizations, all of whom were instrumental in making Madigan Army Medical Center (MAMC) research a resounding success in 2006. We appreciate the support and participation of the Western Regional Medical Center (WRMC) Command Leadership for fostering an environment where "Care with Compassion" is the motto and meticulous scientific process is the standard. We would like to thank our many corporate and industry research sponsors and partners, especially those foundations that foster military, medical research and support the Madigan community. We also would like to acknowledge the dedicated members of the Madigan Institutional Animal Care and Use Committee (IACUC), the Clinical Investigation Committee (CIC), and the Human Use Committee (HUC) whose tireless efforts ensured quality science and ethical conduct of our research. And, last but certainly not least, we would like to thank the hundreds of MAMC's military health care beneficiaries who volunteered to participate in so many demanding research studies, often when the only conceivable benefits were to individuals other than themselves.



## **Foreword**

### **Clinical Studies Service (CSS)**

The Clinical Studies Service has as its mission to increase the quantity and the quality of clinical trials that are open and available to military beneficiaries. This is accomplished by working with investigators in the clinics to determine their research interests, commonly seen disease states, and logistical hurdles to implementing trials. The goal is that each clinic have the support staff necessary to offer patients clinical trial options for most commonly seen diseases.

Successful collaborations over the past year include progress toward participation as the only IRB outside of the National Capitol Area to join the United States Military Cancer Institute IRB. Successes in terms of hiring research personnel include participation with USUHS to provide a 3-year grant to hire a research nurse to the Hematology/Oncology Clinic and offering a contract to a physician-researcher to perform clinical trials within primary care clinics, primarily Internal medicine and Family Practice. Other successes include recruiting clinical trials to multiple specialty services, including Cardiology, Oncology, Orthopedic Surgery, and Cardiothoracic Surgery.

The goals for the next year are to recruit clinical trials to MAMC that will allow hiring of research staff in the Family Medicine, Neurology, and Emergency Medicine services, improve the collaboration with the USMCI, and represent MAMC interests with CIRO in simplifying and standardizing research protocols and IRB practices, with a goal of increasing collaboration between military medical centers.

### **Laboratory Animal Resources Service (LARS)**

LARS remains heavily involved in the trauma training course offered to combat and combat support units of Ft. Lewis and other units under the Western Regional Medical Command. This course has trained over 220 medics, physician assistants, nurses, and doctors in combat trauma management; 64 Emergency Department residents in emergency procedures; 14 urology residents and 24 surgery residents in advanced laparoscopic techniques; and 88 providers in pediatric intubation. LARS has supported the training of more than 72 Special Forces medics. There is increased collaboration between LARS, the Anderson Simulation Center, and the Medical Simulation Training Center to stay current with simulator technology which reduces the number of animals required for effective training. The newt limb regeneration study is ongoing. LARS supports research studies involving cancer metastasis, hypoperfusion/reperfusion injuries, and acute inflammatory reactions. There are new protocols being planned to study effectiveness of a new hemorrhage control material.

### **Research Administration Service (RAS)**

FY06 was a typically busy year for RAS with a total of 127 new protocols and 460 active protocols. New initial and continuing review protocols continued to show 100%

HIPAA compliance. New protocols reviewed at convened IRB meetings averaged less than those in FY05 overall, but the numbers of ERC protocols increased slightly. However, formal research conducted in MAMC and the Western Regional Command Medical continues to be a solid and viable program. No RAS personnel staffing changes have occurred.

The internal audit program continues to be refined, with 21 protocols having been audited. Most audits have shown satisfactory results; however, findings in one instance raised concern about the conduct of retrospective review protocols and the use of subject's protected health information. The number of audits planned during FY07 will be double those conducted in FY06 and will include a few minimal risk retrospective review protocols to ascertain whether the use of codes and the de-linking procedures described in the protocol are being adequately carried out.

The RAS/Protocol Management Quality Improvement Team has continued to refine and implement improvements to local IRB administrative policies and procedures:

1. Updated entire SOP book in preparation for FDA inspection, which RAS is still awaiting.
2. Begun consolidating human use protocol template into one universal format for local and multicenter studies.
3. Turned the Expedited Review Committee (ERC) into a weekly (as needed) meeting for reviewing ERC eligible protocols.

Participated in coordinating 2 semi-annual Applied Research Training (ART) Courses (formerly called Introduction to Clinical Research Course), which are held in collaboration with the MAMC Faculty Development Fellows. Attendance averages about 50 students. Additionally, investigators are still obtaining the required Human Subjects Protections training through DCI's subscription with the University of Miami's Collaborative IRB Training Initiative (CITI).

In FY07, RAS plans to:

- (1) implement a universal human use protocol template;
- (2) continually expand the DCI website to offer more information and reporting options for investigators;
- (3) continue to develop and refine the constructive internal audit program;
- (4) participate in planning the semi-annual ART Course and annual Madigan Research Day;
- (5) work more closely with the Foundations (Geneva, Jackson, and True) to improve communication for the research program;
- (6) host and conduct the annual DCI HELPER Course for research coordinators working within MAMC.

## **Research Operations Service (ROS)**

DCI's Research Operations Service at Madigan Army Medical Center experienced continuing growth in FY 2006. Acquisition of a SELDI-TOF mass spectrophotometer ushered in the official start of high throughput proteomics work at Madigan. The SELDI

technology offers enormous potential for protein biomarker discovery in the analysis of clinical samples and application to ongoing research projects. ROS made significant progress introducing the SELDI-based high throughput proteomic capabilities to MAMC. In our initial longitudinal studies of the human Pregnancy Proteome, study staff enrolled and collected samples at various points of gestation from over 110 patients. ROS also welcomed three new medical technologists to the lab who will be essential in supporting recent increases in GME research activity at MAMC. The laboratory maintained active basic research protocols with 4 of 6 medical departments at MAMC including the departments of Surgery (General Surgery, Urology, and Orthopedics), Pediatrics, Pathology, and OB/GYN (Maternal Fetal Medicine Fellowship). Residents won 2 separate awards at the 9<sup>th</sup> Annual Madigan Research Day for research conducted within the lab. In further support of our GME mission, ROS hosted the 2006 DCI Molecular Biology Short Course. The 5-day lab and lecture course provides novice clinical researchers with perspective on modern molecular and cellular biology techniques and the relationship between basic and clinical research. The ROS laboratory made marked progress on several basic science research protocols including but not limited to the following: a) methods for creating transgenic plants to produce proteins of clinical, environmental and military-unique utility; b) development of cell-based assays against neurotoxins and characterization of G protein coupled receptors using neurons derived from mouse embryonic stem cell culture; c) characterization of the CXCR4/SDF-1alpha chemokine axis as a potential means of directing therapeutic cells to damaged tissue; d) characterization of the molecular mechanisms of limb regeneration in newts. ROS maintained an active internship program with Bates Technical College wherein interns gain valuable real world experience while increasing laboratory productivity. In FY07, ROS looks forward to promoting sustainable and synergistic research efforts among laboratory staff and medical center residents in support of our graduate medical education mission.

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## UNIT SUMMARY - FISCAL YEAR 2006

### A. Objective:

Provide and create an environment to support clinical and basic medical research within Madigan Army Medical Center. Clinical Investigation exists to further the highest degree of medical readiness. DCI supports the Graduate Medical Education mission through leadership in curriculum development, medical education research, and military unique clinical investigations, as well as training opportunities available through institutional programs (ATLS, PALS, etc.).

### B. Technical Approach:

All research, investigational and training activities within the Department of Clinical Investigation are conducted under the guidance of the Office of Human Research Protections (OHRP), Food & Drug Administration (FDA), AR 40-7, AR 40-38, AR 70-25, and AR 40-33. Careful monitoring of all approved protocols is conducted in order to assure strict compliance with the applicable regulations.

### C. Staffing:

Name	Rank	MOS	Title
Amoroso, Paul	COL	61N	Chief, DCI
*Myers, Jerome	COL	61U	Chief, DCI
°McCune, David	LTC	61B	Clinical Trials Director
Arroyo-Ortiz, Lissette	GS11	0671	Health System Specialist
Patience, Troy	GS11	1530	Statistician (Medicine)
Atoigue, Lucy	GS06	0318	Secretary/Steno
Porreca, Mary	GS05	0303	Research Protocol Clerk
Merrill, Nancy	MAJ	64C	Chief, Lab Animal Res Svc
*Gibson, Steven	GS11	0301	Trauma Training Specialist
Karen Van Loon	MSG	91T	Animal Technologist & NCOIC
*Phyll, Shayla	SPC	91T	Animal Technologist
Phillips, Miemie	SPC	91T	Animal Technologist
Spahn-Bridges, Shelley	WG05	5048	Animal Caretaker
*Theis, Jennifer	GS11	0301	Trauma Training Specialist
*McNutt, Patrick	CPT	71B	Chief, Research Op Svc
°Celver, Jeremy	CPT	71A	Cell Biologist
Hartenstine, Michael	CPT	71B	Molecular Biologist
*Fannings, Anthony	SSG	91K	NCOIC
Wright, James	GS11	0644	Medical Technologist
Bullock, Jeff	GS11	0644	Medical Technologist
DeHart, Mary	GS11	0644	Medical Technologist
*Murcin, Lara	GS11	0644	Medical Technologist
*Cederholm, Heidi	GS11	0644	Medical Technologist
*Bergmann, Aspen	GS11	0644	Medical Technologist
*Ippolito, Danielle	GS11	0644	Medical Technologist
Lai, Lonnie	GS13	0601	Chief, Research Administration Svc
Jones, Barbara	GS11	0301	Research Protocol Manager/Auditor
Rayner, Athena	GS09	0303	Research Protocol Specialist
Lund, Jill	GS07	0303	Research Protocol Assistant

#### LEGEND (\*denotes staffing status change)

\*Myers – PCS'd in Jul 2006

\*Phyll – PCS'd in Nov 2006

\*McNutt – PCS'd in Sep 2006

\*Murcin – Resigned in Oct 2005

\*Bergmann – New Hire in Feb 2006

\*Gibson – Resigned in Jan 2006

\*Theis – New Hire/Promotion in Oct 2005/Jul 2006

\*Fannings – PCS'd in Jun 2006

\*Cederholm – New Hire in Feb 2006

\*Ippolito – New Hire in May 2006

°McCune & Celver – Assigned part time

**Summary:**

<u>Personnel:</u>	<u>Authorized</u>	<u>Required</u>	<u>Assigned</u>
Officers	4	4	4
Civilians	17	19	17
Enlisted	4	4	4

**D. Funding:**P8 Funds

Civilian Payroll	\$1,036,814	
Operations	\$149,550	
CEEP	\$286,941	
TDY (CHE)	\$11,290	
TDY (for researchers to present)	\$41,734	
Reproduction Requests	\$1,717	
Contracts	\$7,629	
MEDCASE	\$0	
Military Payroll (est.)	\$558,232	
<b>P8 funds total</b>		<b>\$2,093,907</b>

MAMC Resource Management Division Oversight

Air Force (support for MFM)	\$54,000	
Military units (support for Combat Trauma Training)	\$71,932	
<b>Internal oversight total</b>		<b>\$125,932</b>

Grants Federal

Henry M. Jackson Foundation	\$203,135	
The Geneva Foundation (Tri-Service Nursing)	\$335,362	
T.R.U.E. Foundation	\$964	
<b>Federal grant total</b>		<b>\$539,461</b>

Grants Nonfederal

Henry M. Jackson Foundation (CRADA)	\$146,111	
The Geneva Foundation (CRADA)	\$334,876	
<b>Non-federal grant total</b>		<b>\$480,987</b>

<b>FY06 Research Resources Total</b>		<b>\$3,240,287</b>
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## **E. Progress**

During FY 2006, there were 464 active protocols that received administrative and/or technical support during the year, of these, 317 are presently ongoing, 3 are in a suspended status, 99 were completed, 40 were terminated, 4 are IACUC expired protocols. The principal investigator distribution was as follows: 333 staff protocols, 85 resident protocols, 18 fellow protocols, and 2 Special Forces animal protocols. There were 127 new protocols, of which 10 were Exempt, 59 were ERC, 48 were IRB, and 10 were IACUC protocols.

There were 93 publications in publicly available sources and 163 presentations at regional or national meetings.

## **F. Program Support**

**Programs supported by DCI:** 10 internships, 15 residencies, 5 fellowships, and 7 non-MC programs; they are:

*Internships:* Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Orthopaedic Surgery, Pathology, Pediatrics, and Transitional Year.

*Residencies:* Emergency Medicine, Family Practice, General Surgery, Internal Medicine, Neurology, Obstetrics and Gynecology, Ophthalmology, Oral and Maxillofacial Surgery, Orthopaedic Surgery, Otolaryngology, Pathology, Pediatrics, Preventive Medicine (Public Health), Radiology (Diagnostic), and Urology.

*Fellowships:* Developmental Pediatrics, Faculty Development (Family Practice), Geriatric Medicine, Maternal-Fetal Medicine, and Urogynecology.

*Non-MC programs:* Diabetic Foot Fellowship, Occupational Therapy, Pediatric Psychology, Pharmacy Practice, Physician Assistance Program (Emergency Medicine & Orthopaedics), and Podiatry.

### **Other training protocols supported by DCI:**

DCI: 203023, 203077, 203092, 206109

Department of Surgery: 203016, 204058, 204101, 205017, 205079, 206030

Department of Emergency Medicine: 204028, 206078

Special Forces: 206018, 206106

## **G. Committee Members**

Clinical Investigation Committee  
COL Paul J. Amoroso, MC  
Chairman

Chief or delegated representative of:

Department of Emergency Medicine  
Department of Family Medicine  
Department of Medicine  
Department of Nursing  
Department of OB/GYN  
Department of Pathology  
Department of Pediatrics  
Department of Pharmacy  
Department of Preventive Medicine  
Department of Radiology  
Department of Surgery  
Physical Medicine & Rehabilitation Service  
Department of Clinical Investigation (DCI)  
Clinical Studies Service, DCI  
Medical Statistician, DCI  
Research Administration Service, DCI  
Research Operations Service, DCI  
General Surgery Research Resident, DCI



Human Use Committee  
COL Paul J. Amoroso, MC  
Chairman

Chief or delegated representative of:

- Department of Nursing
- Department of Pathology
- Department of Pediatrics
- Department of Pharmacy
- Department of Radiology
- Department of Ministry and Pastoral Care
- Research Administration Service, DCI
- Social Work Service
- Center Judge Advocate
- Non-institutional Member

Institutional Animal Care & Use Committee  
MAJ Andrew C. Peterson, MC  
Chairman

Chief or delegated representative of:

- Department of Clinical Investigation (DCI)
- Department of Pathology
- Department of Medicine
- Department of Surgery
- Non-affiliated Member and Alternate Non-affiliated Member
- Attending Veterinarian, DCI
- Animal Care Worker, DCI

## **H. Awards**

Each of the following awards was judged based on a submitted manuscript.

### **Major General Byron L. Steger Research Award**

This award is given to a resident, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research

Recipient of this award for 2006: CPT James Wang, MC

Manuscript: *Efficacy of Iron in Patients with Restless Legs Syndrome and a Low-Normal Ferritin: A Randomized, Double-Blind, Placebo Controlled Study*

### **COL Patrick S. Madigan Foundation Research Award**

This award is given to a fellow, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2006: MAJ Jennifer L. Gotkin, MC

Manuscript: *Progesterone Reduces Lipopolysaccharide Induced Interleukin-6 Secretion in Fetoplacental Arteries, Fractionated Cord Blood, and Maternal Mononuclear Cells*

### **Major General Kenyon Joyce Award**

This award is given to staff, submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 2006: LTC Bobby C. Howard, MC, USAF

Manuscript: *A Comparison of Oxytocin Requirements in Patients Randomized to Elective Induction of Labor versus Expectant Management*

## **Madigan Research Day Awards**

These awards are given after Madigan's Annual Madigan Research Day to recognize the best presentation in the each of the following six sessions: Military Unique Clinical Investigation, Medical Education Research, Experimental Design, Managed Care/Health Outcomes, Case Report, and Poster. This year's winners are:

**Military Unique Clinical Investigation** - CPT Julie Ake, MC for presentation entitled "Risk Behavior, Knowledge and Attitudes of ROTC Cadets Regarding HIV/AIDS"

**Medical Education Research (tie)** - MAJ Aaron Saguil, MC for presentation entitled "The Role of Evidence and Other Determinants in Family Medicine Resident Physician Discussions of Spirituality with Patients"

**Medical Education Research (tie)** - MAJ Jean Jones, AN for presentation entitled "Junior Army Nurse Corps (ANC) Officers' Experiences & Expectations of Head Nurse (HN) Leadership"

**Case Report** - CPT Kerry O'Brien, MC for presentation entitled "Managing Patients with Rare Antibodies and Multiple Medical Issues is a Difficult Problem Requiring a Team Approach"

**Experimental Design** - CPT Garth Herbert, MC for presentation entitled "Intraperitoneal LPS Delivery in Mice Causes Multi-organ, Coordinated Modulation of SDF-1 $\alpha$  Production over a 72-Hour Period"

**Managed Care/Outcome Studies** - CPT Jeffrey Tebbs, MS for presentation entitled "Decreasing Behavioral Restraint Use: A Workload Management Approach"

**Poster** - 1LT Robin Smith, AN for presentation entitled "An Evidence-Based Clinical Intervention Strategy to Reduce Falls: The Next Generation"

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**Special awards presented during Madigan Research Day:**

### ***BG GEORGE J. BROWN MENTOR'S CUBE***

The BG George J. Brown Mentor's Cube honors the vital role of the mentor in the process of medical education and research. Madigan Research Day celebrates the breadth and depth of scholarly activity performed at MAMC. The BG George J. Brown Mentor's Cube honors this vital core attribute of excellence in medical scholarship.

**Presented to:** LTC Peter Napolitano, MC

**Department:** Obstetrics/Gynecology

### ***NANCY J. WHITTEN OUTSTANDING IRB MEMBER AWARD***

An IRB is a committee designated by an institution to review, to approve the initiation of, and to conduct periodic review of biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of human subjects. An outstanding IRB member goes the extra mile. This award was created to honor those that contribute above and beyond the call of duty.

**Presented to:** COL Jerome Myers, MC

**Department:** Clinical Investigation

### ***BG MACK C. HILL FACILITATOR'S AWARD***

This award was created to recognize a Madigan member who has helped to facilitate the center's research mission in ways that are not always apparent to the general population. This individual represents the epitome of selfless service through their continual and frequent transparent support of others success .... they exhibit a generous customer service attitude.

**Presented to:** CPT Matthew Miller, JA

**Department:** Center Judge Advocate

### ***BG MICHAEL DUNN 'PRESS-ON' AWARD***

The award is an obelisk which signifies the interconnecting spheres of the physical, mental and spiritual in the human experience. The BG Michael A. Dunn Award recognizes that the attributes of persistence and determination are at least as, and perhaps, more important than talent, genius or education in reaching meaningful goals. This award, established in 2005, is presented annually to a member of the staff whose determination has led to significant contributions in Research, Education, Patient Care and/or Administrative Procedures over the past twelve months.

**Presented to:** CPT Jessica Arens, MS

**Department:** Psychiatry

## **I. Presentations**

### **Department of Clinical Investigation**

Merrill NL. US Army Veterinary Corps. Presented at WSU Swine Center, Pullman, WA, March 2006.

### **Department of Emergency Medicine**

Blankenship RB. Web education: an introduction/overview. Presented at American College of Emergency Physicians Advanced Teaching Fellowship, Albuquerque, NM, September 2006.

Blankenship RB. How to construct an online lecture. Presented at American College of Emergency Physicians Advanced Teaching Fellowship, Albuquerque, NM, September 2006.

Blankenship RB. Deploying your Web training. Presented at American College of Emergency Physicians Advanced Teaching Fellowship, Albuquerque, NM, September 2006.

Blankenship RB. Building Interactive Online Content. Presented at American College of Emergency Physicians Advanced Teaching Fellowship, Albuquerque, NM, September 2006.

Blankenship RB. The Internet as an Educational Tool. Presented at Joint Services Symposium 2006, San Antonio, TX, March 2006.

Blankenship RB. Thrombosis of a Non-ruptured Abdominal Aortic Aneurysm in a 48 year-old Female. Presented at Joint Services Symposium 2006, San Antonio, TX, March 2006.

### **Department of Family Medicine**

Angwafo NN. Management of Cerebrospinal Fluid Rhinorrhea in Pregnancy. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Junnila JL. Do Race or Rank Predict Receipt of Pap Test in a Military Healthcare System? Presented at USAFP Annual Scientific Meeting, Chicago, IL, March 2006.

Pflipsen MC. Vitamin B12 Deficiency in the Type 2 Diabetic Population. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Pflipsen MC, Oh RC, Saguil A. Vitamin B12 Deficiency in the Type 2 Diabetic Population: A Preliminary Report. Presented at USAFP 2006 Annual Meeting and Exposition, Chicago, IL, March 2006.

Runser LA. Esophagogastroduodenoscopy by a Family Physician: A Case Series Demonstrating Healthcare Savings. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Runser LA, Short MW. Upper Endoscopy by a Family Physician. Presented at AAFP National Scientific Assembly, Washington, DC, September 2006.

Saguil AA. Residents and Patient Spirituality. Presented at American Academy of Family Physicians Scientific Assembly, Washington, DC, September 2006.

Saguil AA. The Role of Evidence and Other Determinants in Family Medicine Resident Physician Discussions of Spirituality with Patients. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

## **Medical Education**

Stillsmoking KL. Simulation Education: The Paradigm in Healthcare's Training Process. Presented at ASSN of Perioperative Registered Nurses, Tacoma, WA, April 2006.

### **Internal Medicine Service, Department of Medicine**

Abbott JT, Davis JL. Post operative complication after tricuspid / pulmonmic valve replacement in a patient with metastatic carcinoid syndrome. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Ake JA. Risk Behavior, Knowledge and Attitudes of ROTC Cadets Regarding HIV/AIDS. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Ake JA, Coyle JR, Wojciehowski AO, Morris JT. Risk behavior, knowledge and attitudes of ROTC cadets regarding HIV/AIDS. Presented at Army American College of Physicians Annual Meeting, San Antonio, Tx, November 2005.

Ake JA, Erickson JC, Lowry KJ. Cerebral aneurysmal arteriopathy associated with adulthood HIV infection. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Ake JA, Mysliwiec AG, Mysliwiec V. Intrathoracic granulocytic sarcoma presenting with pleural effusion in a patient with CMML. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Bauler KC, Harner KC, Niven AS. A patient with progressive dyspnea and skin thickening: A treatment dilemma. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Broy CC. Gitelman's Disease in a Patient with Nephrocalcinosis Secondary to Hyperparathyroidism. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Broy CC, Bennett SP. Partial Anomalous Pulmonary Venous Return. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Coyle JR, Harner KC. Dactylitis Secondary to Systemic Lupus Erythematosus. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

DeHaan PJ, Mysliwiec V. An Unusual Case of an Exudative Lymphocyte-Predominant Pleural Effusion. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

DeHaan PJ, Rinard JP, Roth BJ. Dose adherence to the American Thoracic Society (ATS) treatment guidelines for parapneumonic effusions affect outcome? Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

DeHaan PJ, Rinard JP, Roth BJ. Dose Adherence to the American Thoracic Society (ATS) Treatment Guidelines for Parapneumonic Effusions Affect Outcome? Presented at American College of Physicians Annual Meeting, Philadelphia, PA, April 2006.

Feaver AA, Derrick BC, Peterson CK. Results from the diabetes care center: A disease targeting approach. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Feaver AA, Derrick BC, Peterson CK. Results from the diabetes care center: A disease targeting approach. Presented at Army American College of Physicians Annual Meeting, Seattle, WA, November 2005.

Feaver AA, Derrick BC, Peterson CK. Results from the Diabetes Care Center: A Disease Targeted Approach. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Fischer CJ, Gibson CA. Chronic urticaria: Resolution with total thyroidectomy. Presented at Washington State American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Fischer CJ, Peterson CK, Watts JA. Subspecialty elective participation by internal medicine housestaff and ABIM certification examination performance. Presented at SGIM Annual Meeting, Los Angeles, CA, April 2006.

Kiley CA. Use of CT Scan Pulmonary Angiography (CTPA) in the Evaluation of Venous Thromboembolism (VTE): An Examination of Hospital Referral Practices. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Kiley CA, Lowry KJ, Mysliwiec V. Use of CT Scan Pulmonary Angiography (CTPA) in the Evaluation of Venous Thromboembolism (VTE): An Examination of Hospital Referral Practices. Presented at American College of Physicians Annual Meeting, Philadelphia, PA, April 2006.

Kiley CA, Mysliwiec V, Lowry KJ. Use of CTPA in evaluation of venous thromboembolism - an examination of hospital referral practices. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Kwon HP, Lowry KJ. Atypical sepsis in an intravenous drug user. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Kwon HP, Mysliwiec V. A Rare Case of Hemoptysis. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Owshalimpur D, Cushner HM, Lee JY, Starnes BW. Does high resistive index by Doppler ultrasound predict small kidney. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Owshalimpur D, Kunz J, Kenwood B. Percutaneous treatment of a kinked LIMA. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Reilly SC, Lowry KJ. Failed Medical Management of a MRSA Sternoclavicular Septic Arthritis. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Sapp JE, Ake JA, Morris JT, Niven AS, Mysliwiec AG. Metastatic Melanoma in an HIV-Positive 53 year-old-male. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Wang JY. Efficacy of Iron in Patients with Restless Legs Syndrome and a Low-Normal Ferritin: A Randomized, Double-Blind, Placebo Controlled Study. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Wang JY. Efficacy of iron in patients with restless leg syndrome and a low-normal ferritin: a randomized, double-blind, placebo controlled study. Presented at SLEEP 2006 20th Anniversary Meeting of the Associated Professional Sleep Society, Salt Lake City, UT, June 2006.

Wang JY, Fischer CJ, DeHaan PJ, Owshalimpur D, Mysliwiec AG. Efficacy of iron in patients with restless legs syndrome and low-normal ferritin: a randomized, double-blind, placebo controlled study. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Wang JY, McKinley BT, Lee JY. Atypical presentation of Sjogren's syndrome manifesting as acute renal failure. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Wilton NK, Howden JK. Acute pancreatitis in a patient secondary to volvulus after simultaneous pancreas and kidney transplant. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Witters RA, Lowry KJ. Linezolid and atypical mycobacteria. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Witters RA, Morris JT, Mahlen SD. A rare case of sepsis caused by *Erysipelothrix Rhusiopathiae* bacteremia. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

Wojciehowski AO, Rutberg S. Broken Hearts: A Case Series of Catecholamine Induced Cardiomyopathy and Literature Review. Presented at Army American College of Physicians Annual Meeting, San Antonio, TX, November 2005.

## **Neurology Service, Department of Medicine**

Flynn FG. Update on Normal Pressure Hydrocephalus. Presented at 25th Annual AMEDD Neurology Conference, San Antonio, TX, November 2005.

Hohler AD. Domestic Violence Education and Practice Improvement. Presented at American Academy of Neurology, San Diego, CA, April 2006.

Hohler LD. Parkinsonism Related to Oral Ingestion of Manganese. Presented at American Academy of Neurology, April 2006.

Lee JD. Neurological Perspectives in End of Life Care. Presented at Washington State Medical Association Annual Meeting, Seattle, WA, September 2006.

Lee JD. Neurological Complications of Thermal Injury. Presented at American Academy of Neurology, San Diego, CA, April 2006.

Scott BR. Horner Syndrome. Presented at Pacific Northwest Neuro-Ophthalmology Society Meeting, Casey Eye Institute, Portland, OR, November 2005.

Theeler BJ. Prevalence and Impact of Migraine among U.S. Army Soldiers Deployed to a Combat Theater. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Theeler BJ, Mercer R, Erickson JC. Prevalence and Impact of Migraine Among U.S. Soldiers Deployed to a Combat Theater. Presented at American Headache Society Annual Meeting, Los Angeles, CA, June 2006.

## **Department of Nursing**

Bryant JV. The Effects of St. John's Wort on Emergence Time from General Anesthesia in Male Sprague-Dawley Rats (*Rattus norvegicus*) Undergoing Abdominal Surgery. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Carney LM. Call to duty: NP's on the Front Lines. Presented at AANP, June 2006.

Garner BK. ICU Restraint Protocol Initiative and Compliance in the Intensive Care Units. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Hopkins DL. Stress, Role Strain, Health & Attrition in Junior Enlisted Air Force Women with and without Preschool Children. Presented at 38th Biennial Sigma Theta Tau International Convention, Indianapolis, ID, November 2005.

Jones JM. Junior Army Nurse Corps (ANC) Officers' Experiences & Expectations of Head Nurse (HN) Leadership. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.



Jones JM, Loan LA, Cofield TS, Blackman LL. Junior ANC Officers' Experiences & Expectations of Head Nurse Leadership. Presented at Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, May 2006.

Kamara J. The Impact of Inpatient Physician Order Entry on Medication Administration Error Rates in the Neonatal Intermediate and Intensive Care Units. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Raymond SM. From Numbers to Knowledge to Know-How: Using Pressure Ulcer Prevalence Data to Improve Patient and Cost Outcomes. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Reyes SD, Looper R. Academic Readiness and Board of Nursing Examiners Brief. Presented at AMEDD C & S Fort Sam Practical Nurse Educators Conference, San Antonio, TX, August 2006.

Ribbing SK. Effects of Chrysin on Emergence Time in Sprague-Dawley Rats after Laparotomy. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Serna ED. A Continuous Quality Improvement Project to Examine and Enhance Nurse's Management of Tube Feedings. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Smith RD. An Evidence-Based Clinical Intervention Strategy to Reduce Falls: The Next Generation. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Tebbs JS. Decreasing Behavioral Restraint Use: A Workload Management Approach. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

### **Anesthesia Students, Department of Nursing**

Andalis MA, Ribbing SK, Weston EM. The Effects of Chrysin, a Passiflora Incarnata Extract, on Emergence Time from Anesthesia in Male Sprague-Dawley Rats after Intra-abdominal Surgery. Presented at Annual Meeting, American Association of Nurse Anesthetists, Cleveland, OH, August 2006.

Bryant JV, Frondozo RR, King TL, Robinson JS. The Effects of St. John's Wort on Emergence Time from General Anesthesia in Sprague-Dawley Rats (*Rattus norvegicus*) Undergoing Abdominal Surgery. Presented at Annual Meeting, American Association of Nurse Anesthetists, Cleveland, OH, August 2006.

Downs AM. Efficacy of Preoperative Valerian on Day of Surgery Anxiety. Presented at Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, May 2006.

Harm PS. Infection with Epidural Placement the Role of Asepsis in Reducing the Incidence of Infections Complications. Presented at Washington Association of Nurse Anesthetists, Seattle, WA, April 2006.

Kondrat PM. Current Perioperative Issues: Battlefield Lessons Learned. Presented at 8th Annual TriService Perioperative Nursing Symposium, Washington, DC, March 2006.

Whitacre WC. Anesthesia in an Austere Environment: Afghanistan. Presented at Washington Association of Nurse Anesthetists, Seattle, WA, April 2006.

Wulf PM, Long AL, Arredondo A, Petty LA, Marshall WB, Reilly M. The Laryngeal Mask Airway: Comparison of Two Insertion Techniques and Waste Anesthetic Gas Leakage. Presented at American Association of Nurse Anesthetists, November 2005.

Zwerling A, Fish D. Approaching the Patient with the Difficult Airway. Presented at Washington Association of Nurse Anesthetists, Seattle, WA, April 2006.

## **Nursing Research Service, Department of Nursing**

Argueta SJ. Nursing Workload Data Collection in the Post Anesthesia Care Unit. Presented at Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, May 2006.

Hemman EA. Evaluation of the Semi-Annual Combat Medic Skills-Validation Test (SACMS-VT). Presented at Tri-Service Nursing Research Conference: 13th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, April 2006.

Hemman EA. Evaluation of the Semi-Annual Combat Medic Skills-Validation Test. Presented at Tacoma General (Multicare), Tacoma, WA, June 2006.

Hopkins DL. Stress, Role Strain, Health & Military Career Aspiration in Junior Enlisted AirForce Women With & Without Preschool Children. Presented at 14th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, May 2006.

Ketz AK. The Experience and Management of Phantom Limb Pain in Patients with Traumatic Amputation Resulting from Combat or Training Injury. Presented at Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, May 2006.

Loan LA, Whitney D, Taylor JA. The Impact of Inpatient Physician Order Entry on Medication Administration Errors Rates in the Neonatal Intermediate & Intensive Care Units. Presented at Phyllis J. Verhonick Nursing Research Conference, San Antonio, TX, May 2006.

McCarthy MS, Simonson K, Sorensen D, Bamgartner B, Demars S. Perioperative Immunonutrition for Head and Neck Cancer: A Feasibility Study. Presented at 14th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, May 2006.

Schlicher ML. It's a Small World After All... Using Nanotechnology in Nursing & Medicine. Presented at 2006 National Conference of the American Association of Critical Care Nurses, Anaheim, CA, May 2006.

Smith RD. An Evidence-Based Clinical Intervention Strategy to Reduce Falls: The Next Generation. Presented at 14th Biennial Phyllis J. Verhonick Nursing Research Course, San Antonio, TX, May 2006.

Trego LL. Military Women's Thoughts on Menstruation and Menstrual Suppression During Deployment. Presented at Pacific Nursing Research Conference, Honolulu, HI, February 2006.

Trego LL. Military Women's Thoughts on Menstruation and Menstrual Suppression During Deployment. Presented at The Association of Women's Health, Obstetric, and Neonatal Nurses (AWHONN), Baltimore, MD, June 2006.

## **Department of Obstetrics/Gynecology**

Buchard E, Deering SH, Kuskowski LJ, Miller C, Driggers R. Incidental finding of angular pregnancy delivered at 35 weeks for oligohydramnios: A case report and literature review. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Burris AC. Resident Training in Assessment of the Sexual Assault Patient Utilizing Simulation. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Burris AC, Deering SH, Chinn M. Resident Training in Assessment of the Sexual Assault Patient Utilizing Simulation. Presented at Council on Resident Education in OB/GYN (CREOG) and The Association of Professors of Gynecology and Obstetrics (APGO) Annual Meeting, Orlando, FL, March 2006.

Burris AC, Shields AD, Deering SH. Ovarian Vein Thrombosis in Early Pregnancy. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, November 2005.

Deering SH. Simulation Training for Postpartum Hemorrhage. Presented at Council on Resident Education in Obstetrics and Gynecology (CREOG) and The Association of Professors of Gynecology and Obstetrics (APGO) Annual Meeting, Orlando, FL, March 2006.

Deering SH. Interactive Simulation Technologies in OB/GYN: Simulation Symposium. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Gotkin JL. Progesterone Reduces Lipopolysaccharide Induced Interleukin-6 Secretion in Fetoplacental Arteries, Fractionated Cord Blood, and Maternal Mononuclear Cells. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Gotkin JL, Flood SK, Deering SH. A new case of an old problem: A case report of sepsis resulting from attempted self-termination. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Gotkin JL, McNutt PM, Cerver JP, Shields AD, Wright JR, Hoeldtke NJ, Napolitano PG. Progesterone Reduces Lipopolysaccharide Induced Inflammatory Cytokine Secretion in Fetoplacental Arteries and Fractionated Cord Blood. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Gotkin JL, McNutt PM, Cerver JP, Shields AD, Wright JR, Hoeldtke NJ, Napolitano PG. Progesterone Reduces Lipopolysaccharide Induced Inflammatory Cytokine Secretion in Fetoplacental Arteries and Fractionated Cord Blood. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Gotkin JL, McNutt PM, Cerver JP, Shields AD, Wright JR, Hoeldtke NJ, Napolitano PG. Progesterone Reduces Lipopolysaccharide Induced Inflammatory Cytokine Secretion in Fetoplacental Arteries and Fractionated Cord Blood. Presented at 26th Annual Meeting of the Society for Maternal-Fetal Medicine, Miami, FL, February 2006.

Gotkin JL, Shields A, Napolitano P, McNutt P, Cerver J, Wright J. Progesterone Reduces Lipopolysaccharide Induced Inflammatory Cytokine Secretion in Fetoplacental Arteries & Fractionated Cord Blood. Presented at Society for Maternal Fetal Medicine Annual Meeting, Miami, FL, February 2006.

Guidry BA, Napolitano PG. Screening for Depression at Postpartum Appointments. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Han JJ, Shen-Gunther J. Accuracy of Office Endometrial Biopsy: Comparison of Biopsy and Hysterectomy Findings. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

Paonessa DJ. 17-Hydroxyprogesterone Caproate Reverses Thromboxane Induced Vasoconstriction of Fetal-Placental Arteries in the Ex Vivo Placental Cotyledon Model. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Paonessa DJ, Napolitano PG, Shields AD, Cerver JP, Howard BC, Gotkin JL, Deering SH, Hoeldtke NJ. The Effect of Cholic Acid on Placental Artery Perfusion Pressure in the Ex-Vivo Placental Cotyledon Model. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Paonessa DJ, Shields AD, Cerver JP, Howard BC, Gotkin JL, Hoeldtke NJ, Napolitano PG. 17-P Hydroxyprogesterone Caproate Reverses Thromboxane Induced Vasoconstriction of Fetoplacental Arteries in the Ex-Vivo Placental Cotyledon Model. Presented at 44th Annual Armed Forces

District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Saunders RD, Thomson SB, Shields AD. Renal Tubular Acidosis Presenting as Hypokalemia in Pregnancy: A Case Report and Review of Literature. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

Sessions DC, Napolitano PG. Birth weight and macrosomia: Army versus Navy in the Puget Sound. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

Shen-Gunther J. Hereditary Cancer Genetic Testing: Referral Patterns and Outcomes. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

Shen-Gunther J. Extreme Drug Resistance Assay of Transitional Cell Ovarian Carcinoma. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

Shen-Gunther J. Does Early Treatment with Pegylated Liposomal Doxorubicin Improve Survival Compared to Topotecan in Patients with Recurrent Ovarian Cancer? Presented at Society of Gynecologic Oncologists 2006 Annual Meeting, Palmsprings, CA, March 2006.

Shields AD, Hill DL. Management of Aplastic Anemia Diagnosed in Pregnancy: A Case Report and Review of the Literature. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Temple ST, Shields AD. Fatal Congenital Cardiomyopathy in Type I Myotonic Dystrophy. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Wakefield CL. GIST (Gastrointestinal Stromal Tumor) of the Vagina. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

Wilson KL, Lattu AL, Lucas W. Incisional Endometrioma Following Cesarean Delivery. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

You W, Driggers R, Bobo W, Deering SH. Treatment of anorexia nervosa in pregnancy: A case report and review of the literature. Awarded Outstanding Poster. Presented at 44th Annual Armed Forces District Meeting of the American College of Obstetricians & Gynecologists, Seattle, WA, November 2005.

Zalucki CM. Paroxysmal Nocturnal Hemoglobinuria in Pregnancy. Presented at Annual ACOG Armed Forces District Meeting, Seattle, WA, October 2005.

## **Department of Pathology**

O'Brien KL. Three Unusual Histologic Variants of Fibrous Papule. Presented at International Society of Dermatopathology 9th Joint Meeting, San Francisco, CA, March 2006.

O'Brien KL. Managing Patients with Rare Antibodies and Multiple Medical Issues is a Difficult Problem Requiring a Team Approach. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

## **Department of Pediatrics**

Benton KB. A Case Report of an Isolated, Midline Facial Cutaneous Appendage: An Uncommon Example of Disorganization in Humans. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Cornfeld RJ. Juvenile Arthritis Presenting as a Soft Tissue Mass. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Eigner DJ. Epstein-Barr Virus presenting as genital ulcers. Presented at Uniformed Services Pediatric Seminar, Portsmouth, VA, March 2006.

Eigner DJ. Epstein-Barr Virus Infection Presenting as Genital Ulcers. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Fairchok MP. Pandemic Influenza - Not just for the birds. Presented at , Portsmouth, VA, March 2006.

Flake EM. Aortic Root Dilatation in a Patient with Overlapping Osteogenesis Imperfecta/Ehlers-Danlos Syndrome Phenotype. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Stephan MJ, Benton KB, Holm MT, Gries DM. Congenital Midline Facial Cutaneous Appendage: Pathological Manifestations of Disorganization in Humans. Presented at XXVII David W. Smith Workshop on Malformations and Morphogenesis, Lake Arrowhead, CA, September 2006.

## **Department of Preventive Medicine**

Moore CA, Berke E, Cherutich P, Reed S. Elective Primary Cesarean Delivery in Washington State: The Insurance Factor. Presented at 12th Annual Joint Conference on Health - Partnering for a Healthier Tomorrow, February 2006.

Ross TW. Hearing Loss in the Military: The Results of Deployment to a Combat Environment. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Ross TW, Johnson R, Opheim G. Informatics and STD surveillance - a software application for reporting and managing sexually transmitted diseases. Presented at Preventive Medicine 2006, Reno, NV, February 2006.

Ross TW, Wiesen AR, Daniell W. Hearing Loss in the Military: The Results of Deployment to a Combat Environment. Presented at National Occupational Research Agenda Symposium 2006, Washington DC, April 2006.

## **Department of Psychology**

Gahm GA. Post-Deployment Health Re-Assessment (PDHRA). Presented at Force Health Protection 2006, Albuquerque, NM, August 2006.

Gahm GA, Meyer JG, Miller JL, Lucenko BA. The Soldier Wellness Assessment Pilot Program at Ft. Lewis. Presented at Force Health Protection 2006, Albuquerque, NM, August 2006.

Lucenko BA. Screening for Mental Health Problems Following Deployment. Presented at Society for Traumatic Stress Studies, Toronto, Canada, November 2005.

Peterson KA, Knauss LG. The Use of Prazosin in the Treatment of Combat-Related Nightmares in Active Duty Soldiers. Presented at Albuquerque Convention Center, Albuquerque, NM, August 2006.

## **General Surgery Service, Department of Surgery**

Arthurs ZM. The Impact of Hypothermia on Trauma Care at the 31st Combat Support Hospital in Iraq. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Arthurs ZM. RAS. Presented at Gary P. Wratten Army Surgical Symposium, Washington, DC, May 2006.

Arthurs ZM, Cuadrado DG, Beekley AC, Grathwohl KW, Sebesta JA, Rush RM. The Impact of Hypothermia on Trauma Care at the 31st Combat Support Hospital in Iraq. Presented at North Pacific Surgical Association, Vancouver, BC, Canada, November 2005.

Beldowicz BC. Combat Vascular. Presented at Gary P. Wratten Army Surgical Symposium, Washington, DC, May 2006.

Cronk DR, Houseworth TP, Herbert GS, Cuadrado DG, Azarow KS. Intestinal Fatty Acid Binding Protein (I-FABP) for the Detection of Strangulated Mechanical Small Bowel Obstruction. Presented at Pacific Coast Surgical Association 77th Annual Meeting, San Francisco, CA, February 2006.

Cuadrado DG. 31st CSH Cause of Death. Presented at Gary P. Wratten Army Surgical Symposium, Washington, DC, May 2006.

Eckert MJ, Azarow KS. Bronchoscopy in the Blast Injured Patient. Presented at Pacific Coast Surgical Association 77th Annual Meeting, San Francisco, CA, February 2006.

Herbert GS. Intraperitoneal LPS Delivery in Mice Causes Multi-organ, Coordinated Modulation of SDF-1? Production over a 72-Hour Period. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Herbert GS. SDF-1. Presented at Gary P. Wratten Army Surgical Symposium, Washington, DC, May 2006.

Martin MJ. Pediatric Monitoring. Presented at San Antonio Trauma Symposium, San Antonio, Tx, September 2006.

McGuigan RM, Spinella PC, Beekley A, Sebesta J, Perkins J, Grathwohl K, Azarow K. Pediatric Trauma: Combat Support Hospital Experience in Iraq. Presented at American Pediatric Surgical Association, South Carolina, May 2006.

Mullenix PS. MODS. Presented at Gary P. Wratten Army Surgical Symposium, Washington, DC, May 2006.

Sohn VY. Combat Vascular. Presented at Gary P. Wratten Army Surgical Symposium, Washington, DC, May 2006.

Sohn VY, Rush RM, Sebesta JA, Beekley AC, Gibson SO, Azarow KS, Koeller CA, Meyer JG. From Buddy-aid to the Forward Surgical Team: The Madigan Model for Improving Trauma Readiness of Brigade Combat Teams Fighting the Global War on Terror. Presented at 1st Annual Academic Surgical Conference, San Diego, CA, February 2006.

### **Ophthalmology Service, Department of Surgery**

Davis RW. LASIK Flap Stability in Ocular Trauma. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Frazier TC, Nelson ML. Case Series Late - Onset Corneal Haze > 10 months after Photo Retractive Keratectomy (PBK) in Soldiers Deployed to Afghanistan. Presented at Annual Symposium American Society, San Francisco, CA, March 2006.

### **Orthopedics Service, Department of Surgery**

Gloystein DM. Developmental Dislocation of the Hip: A Long-Term Treatment Outcomes Study. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Gloystein DM, Grassbaugh JA, Arrington ED. PCL Tunnel Lengths, An Anatomic Study. Presented at The American Academy of Orthopaedic Surgery, Annual Meeting, Chicago, IL, March 2005.

Guzzo JA, Herzog JP, Arrington E, Devine J. A Retrospective Review of Injuries Sustained During OIF and OEF Treated at a Tertiary Military Medical Center. Presented at Washington State Chapter of American College of Surgeons, Sun River, OR, June 2006.

Herzog JP, Arrington ED, Devine JG, Bluman EM. A Field Expedient Wound Vacuum System. Presented at Washington State Chapter of American College of Surgeons, Sun River, OR, June 2006.

Ryan PM. The Role of the Triradiate Cartilage in Predicting Curve Progression in Adolescent Idiopathic Scoliosis. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

### **Otolaryngology Service, Department of Surgery**

Demars SM. Perioperative Immunonutrition in Head and Neck Cancer. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Demars SM, Harsha WJ, Crawford JV. Effects of Smoking on Rate of Post-Tonsillectomy Hemorrhage. Presented at AAO-HNS Annual Meeting & Oto Expo, Toronto, CA, September 2006.

Poss JM. Post-Tympanostomy Swimming Precautions: A Physician Survey. Presented at AAO-HNS Annual Meeting & Oto Expo, Toronto, Canada, September 2006.

Spear SA. Review of Thyroid Cancer Treatment Outcomes at a Major Medical Center from 1996-2000. Presented at AAO-HNS Annual Meeting & Oto Expo, Toronto, Canada, September 2006.

Spear SA. Thyroid Cancer Treatment Outcomes at a Major Medical Center. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

### **Urology Service, Department of Surgery**

DeCastro BJ. Five Year Follow-up of Asymptomatic Men found to have Testicular Microlithiasis in a Large Screening Study. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

Pugliese JM. The Epidemiology of Nephrolithiasis in Soldiers Returning from Operation Iraqi Freedom. Presented at 9th Annual Madigan Research Day, Tacoma, WA, April 2006.

## **J. Publications**

### **Hospital Dental Clinic**

Viehweg TL. Melanoma of the Oral and Maxillofacial Region. Oral and Maxillofacial Surgical Knowledge Update 2006.

Viehweg TL, Hudson JW. Pneumosinus dilans of the Maxillary Sinuses, Bilaterally: A Case Report. Journal of Oral and Maxillofacial Surgery 64(4): p. 726-30, 2006.

### **Department of Emergency Medicine**

Billingsley RA, Keilman CG. Images in Emergency Medicine: Fournier's gangrene. Ann Emerg Med 47(1): p. 11,21, 2006.

Blankenship RB. Six Steps to Buying Your First or Next PDA. ACEP News 2005.

Brandt AL, Tolson D. Missed abdominal ectopic pregnancy. J Emerg Med 30(2): p. 171-4, 2006.

Johnston GM, Denny MA, Howden J. Herpes Simplex Esophagitis in an Immunocompetent 20 year-old male. Resident and Staff Physician 2006.

Johnston GM, Wilson K, Harrison B. Images in Emergency Medicine: 21 year old female with chronic constipation. Annals of Emergency Medicine 2006.

Murphy CS, Parsa T. Idiopathic Ovarian Vein Thrombosis a Rare Cause of Abdominal Pain. Am J Emerg Med 24(5): p. 636-7, 2006.

Nielson AS, Kang CS. Images in emergency Medicine. Chokehold Strangulation. Ann Emerg Med 47(4): p. 327, 343, 2006.

Wedmore IS, McManus JG, Pusateri AE, Holcomb JB. A Special Report on the Chitosan-based Hemostatic Dressing: Experience in Current Combat Operations. J Trauma 60(3): p. 655-8, 2006.

Wills BK, Mycyk MB, Mazor S, Kanter-Zell M, Brace L, Erickson T. Factitious Lithium Toxicity Secondary to Lithium Heparin-Containing Blood Tubes. Journal of Medical Toxicology 2(2): p. 61-3, 2006.

### **Department of Family Medicine**

Aplund C, Webb C, Barkdull T. Neck and back pain in bicycling. Curr Sports Med Rep 4(5): p. 271-4, 2005.

Edwards JA. Disposal of Unused and Expired Medications by Patients. NAPCRG 2005.

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**K. Exempt Protocols approved in FY 2006 (no detailed summary sheet)**

<b>Number</b>	<b>PI</b>	<b>Dept/Serv</b>	<b>Protocol Title</b>
206090	LaVan JT	FM	Identification of Health Factors Associated with Perceived Quality of Life in an Aging Population
206017	Saguil AA	FM	Physician Perception of the Impact of a Morning Report Educational Intervention
206046	Hopkins-Chadwick DL	Nurs	A Descriptive Study of Military Women's Information Needs for Sexual Health Promotion
206007	Guidry BA	OB	Screening for Depression at Postpartum Appointments
206005	Han JJ	OB	Accuracy of Office Endometrial Biopsy: Comparison of Biopsy and Hysterectomy Findings
206001	Sessions DC	OB	Birth Weight and Macrosomia: Army Versus Navy in the Puget Sound
206003	Shen-Gunther J	OB	Cancer Genetic Testing: Referral Patterns and Outcomes
206065	Whitacre RM	Path	Post Approval Surveillance Study of Platelet Outcomes, Release Tested
206060	Eichinger JK	Surg/Orth	Analysis of Failure Characteristics of Fixed Locking Plates With and Without Screw- Hole Inserts: A Biomechanical Study
206089	Schweinberger MH	Surg/Vas	Foot Care Knowledge of Diabetic Patients in a Military Medical Center

## L. Detail Summary Sheets

## Table of Contents for Detail Summary Sheets

**Legend:**

S = **Status** [O – Ongoing, C – Completed, E – Expired, T – Terminated]

**T = Protocol Type** [A – Animal, B – Bench, C – Cancer, L – Local, M – Multicenter]

<u>Prin. Invest.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
<u>#Protocol No.</u>			

## DEPARTMENT OF ANESTHESIA &amp; OPERATIVE SERVICES

Miller JP #206121	O M	Comparison of Direct Versus Indirect Laryngeal Views using the Video Laryngoscope During Standard Intubation Procedures
Miller JP #204010	C L	Evaluation of the Combat Medic Skills Validation Test

## DEPARTMENT OF CLINICAL INVESTIGATION

Bullock JM #203122	E	A	Establishment of a Limb Regeneration Program Using Notophthalmus viridescens (newt) as the Model Organism and the Creation of a Transgenic N. viridescens Strain
Bullock JM #206122	O	A	Profiling of Proteins Extracted from Tissue Taken from Regenerating and Intact Notophthalmus viridescens Limbs Using SELDI
Hartenstine MJ #205031	O	L	Proteomic Analysis of Longitudinally-Collected Maternal Plasma Samples: Establishing the 'Pregnancy Proteome'
McNutt PM #205044	O	L	A Prospective Study of Pseudocholinesterase Activity in Patients with Fibromyalgia, Chronic Pain, Pelvic Pain and Hernias
Merrill NL #203092	E	A	Animal Tissue Use in Biomedical Research and Training
Merrill NL #206109	O	A	Animal Tissue Use in Biomedical Research and Training
Merrill NL #203076	T	A	Breeding Colony of Red-Spotted Newt (Notophthalmus viridescens)
Merrill NL #206091	O	A	MAMC Rodent and Rabbit Quality Assurance and Sentinel Program
Merrill NL #203075	T	A	Mouse (Mus Musculus) Breeding Protocol

**HOSPITAL DENTAL CLINIC**

Burgan SC O M Host Response Gene 203014 in Military Populations  
#203116

## DEPARTMENT OF EMERGENCY MEDICINE

Cooper JL #204087	T L	A Prospective Study on the Effects of Ginkgo Biloba on Bleeding Times
Denny MA #206063	O L	A Randomized Study of Capnography in Emergency Department Procedural Sedation
Denny MA #206050	T L	Magnesium Sulfate for the Prevention of Etomidate Induced Myoclonus in Emergency Department Procedural Sedation

<u>Prin. Invest.</u> <u>#Protocol No.</u>	<u>S</u>	<u>T</u>	<u>Title</u>
Johnston GM #206028	C	L	Application of the Wells Criteria to determine Pretest Probability of Pulmonary Embolism: A Retrospective Review of the practices of the Madigan Army Medical Center Department of Emergency Medicine
Nielson AS #206059	O	L	Causes and consequences of patients who left a busy Army Medical Center Emergency Department prior to evaluation by a qualified health care provider
Younggren BN #206078	O	A	Emergency Medicine/Combat Trauma Management Training Using Animal Models (Domestic Goat/ Capra hircus, Pig/Sus scrofa)

#### **DEPARTMENT OF FAMILY MEDICINE**

Clark GW #205133	O	L	Prevalence of Hypertension in Active Duty Service Members
Crosland T #205124	O	L	Racial Differences in Health Outcomes for Adults with Diabetes in a Military Setting
Flynn DM #204117	O	L	Impact of the Sole Prescriber Program on use of Opioid Medications and Quality of Life
Flynn DM #206105	O	L	Implementation of an Office-Based Screening Tool to Improve Adherence with Recommended Preventive Services in Primary Care
Kelly KM #205130	O	L	Use of Pedometers Among Healthcare Providers in a Large Military Family Medicine Department
Kimmer SL #206019	C	L	Pediatric Obesity in a Military Family Medicine Clinic
Maurer DM #206048	O	L	A Randomized, Controlled Trial of Manual/Manipulative Therapy for Acute Low Back Pain in Active Duty Military Personnel: A Pilot Study
Pflipsen MC #205025	C	L	Prevalence of Vitamin B12 Deficiency in the Type 2 Diabetic Population
Rosen IM #206067	C	L	Determinants of Military Medical Student Interest in Family Medicine
Saguil AA #205103	C	M	The Role of Evidence and Other Determinants in Resident Discussions of Spirituality with Patients
Sams RW #206104	O	L	Implementing a Medical Ethics Curriculum in a Family Medicine Residency: Assessment of Need, Description of the Process, and Evaluation of Effectiveness
Short MW #205132	C	L	Colonoscopy by a Family Physician: A Case Series Demonstrating Healthcare Savings
Short MW #205131	C	L	Esophagogastroduodenoscopy by a Family Physician: A Case Series Demonstrating Healthcare Savings
Short MW #206080	O	L	Predicting Intern Performance using an Objective Structured Clinical Examination

#### **GRADUATE MEDICAL EDUCATION**

Boden JH #205090	O	L	Attitudes and Perceptions of Refractive Surgery Among ROTC Cadets Presenting for a Flight Physical and Self-Reported Barriers Towards Having Refractive Surgery to Correct Visual Acuity and Becoming Medically Qualified for Army Aviation
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#### **HEALTH OUTCOMES MANAGEMENT DIVISION**

Meyer JG #205108	O	L	The Deployment of Physical Therapy for Combat: A Description of the Process and Outcomes
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<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b><u>Title</u></b>
Daniels JT #93032	O	S	SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation or Stem Cell Transplantation as Adjuvant Intensification Therapy Following Conventional Adjuvant Chemotherapy in Patients with Stage II and III Breast Cancer at High Risk of Recurrence
Daniels JT #93097	O	S	SWOG 9205: Central Prostate Cancer Serum Repository Protocol
Daniels JT #93136	O	S	SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer
Daniels JT #93166	O	S	SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer
Daniels JT #94170	T	S	SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast Cancer Patients with 0-3 Positive Nodes
Daniels JT #95003	O	S	SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer
Daniels JT #95093	O	S	SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas
Daniels JT #94163	O	S	SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study
Daniels JT #96095	O	S	SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary Lymph Nodes and Positive Receptors, Intergroup
Daniels JT #96118	O	S	SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck
Daniels JT #98112	O	S	SWOG C9581: Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-1A Versus No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma
Daniels JT #99014	O	S	SWOG C9741: A Randomized Phase III Trial of Sequential Chemotherapy Using Doxorubicin, Paclitaxel, and Cyclophosphamide, or Concurrent Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer
Daniels JT #200036	O	S	SWOG E1199: A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive Breast Cancer
Daniels JT #99071	O	S	SWOG E2197: Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytosan for the Adjuvant Treatment of Node Positive or High Risk Node Negative Breast Cancer

<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b>Title</b>
Daniels JT #204066	O	S	SWOG E2496 Randomized Phase III Trial of ABVD Versus Stanford V +/- Radiation Therapy in Locally Extensive and Advanced Stage Hodgkin's Disease With 0-2 Risk Factors
Daniels JT #200040	O	S	SWOG E4494: Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma
Daniels JT #202010	O	S	SWOG E5597: Phase III Chemoprevention Trial of Selenium Supplementation in Persons with Resected Stage I Non-Small Cell Lung Cancer
Daniels JT #202012	O	S	SWOG GO182: A Phase III Randomized Trial of Paclitaxel and Carboplatin Versus Triplet or Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Carcinoma
Daniels JT #97070	O	S	SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour
Daniels JT #99040	O	S	SWOG JMA.17: A Phase III Randomized Double-Blinded Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen
Daniels JT #200120	O	S	SWOG N9831: Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel With or Without Trastuzumab as Adjuvant Treatment for Women with HER-2 Over-expressing or Amplified Node Positive or High-Risk Node Negative Breast Cancer (an Intergroup Study)
Daniels JT #201136	C	S	SWOG S0009: A Phase II Evaluation of Neoadjuvant Chemotherapy, Interval Debulking Followed by Intraperitoneal Chemotherapy in Women with Stage III and IV Epithelial Ovarian Cancer, Fallopian Tube Cancer or Primary Peritoneal Cancer
Daniels JT #201137	O	S	SWOG S0012: A Comparative Randomized Study of Standard Doxorubicin and Cyclophosphamide Followed by Weekly Paclitaxel Vs. Weekly Doxorubicin and Daily Oral Cyclophosphamide Plus G-CSF Followed by Weekly Paclitaxel as Neoadjuvant Therapy for Inflammatory and Locally Advanced Breast Cancer
Daniels JT #203084	O	S	SWOG S0016, A Phase III Trial of CHOP + Rituximab vs. CHOP + Iodine-131-Labeled Monoclonal Anti-B1 Antibody (Tositumomab) for Treatment of Newly Diagnosed Follicular Non-Hodgkin's Lymphomas
Daniels JT #204052	C	S	SWOG S0023, A Phase III Trial of Cisplatin/Etoposide/Radiotherapy with Consolidation Docetaxel Followed by Maintenance Therapy with ZD1839 or Placebo in Patients With Inoperable Locally Advanced Stage III Non-Small Cell Lung Cancer
Daniels JT #204123	O	S	SWOG S0106, A Phase III Study of the Addition of Gemtuzumab Ozogamicin (Mylotarg®) Induction Therapy Versus Standard Induction With Daunomycin and Cytosine Arabinoside Followed by Consolidation and Subsequent Randomization to Post-Consolidation Therapy With Gemtuzumab Ozogamicin (Mylotarg®) or No Additional Therapy for Patients Under Age 56 With Previously Untreated DeNovo Acute Myeloid Leukemia (AML)

<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b>Title</b>
Daniels JT #204034	O	S	SWOG S0221, Phase III Trial of Continuous Schedule AC + G Vs. Q 2 Week Schedule AC, Followed by Paclitaxel Given Either Every 2 Weeks or Weekly for 12 Weeks as Post-Operative Adjuvant Therapy in Node-Positive or High-Risk Node-Negative Breast Cancer
Daniels JT #204094	O	S	SWOG S0226, Phase III Randomized Trial of Anastrozole Versus Anastrozole and Fulvestrant as First Line Therapy for Post Menopausal Women With Metastatic Breast Cancer
Daniels JT #204064	O	S	SWOG S0230, Phase III Trial of LHRH Analog Administration During Chemotherapy to Reduce Ovarian Failure Following Chemotherapy in Early Stage, Hormone- Receptor Negative Breast Cancer
Daniels JT #206068	O	S	SWOG S0520: Phase II Study of PXD101 (NSC-726630) in Relapsed and Refractory Aggressive B-Cell Lymphomas
Daniels JT #91094	O	S	SWOG S9007 (ECOG S9007), Cytogenetic Studies in Leukemia Patients
Daniels JT #99019	O	S	SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool
Daniels JT #205035	O	S	SWOG S9910 Leukemia Centralized Reference Laboratories and Tissue Repositories, Ancillary
Daniels JT #200084	O	S	SWOG S9921: Adjuvant Androgen Deprivation versus Mitoxantrone plus Prednisone plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III
Daniels JT #202074	O	S	SWOG S9925 Lung Cancer Specimen Repository Protocol, Ancillary
McCune DE #204073	O	M	A Multicenter, Randomized, Phase III Study of Rituximab versus Iodine I 131 Tositumomab Therapeutic Regimen for Patients with Relapsed Follicular Non-Hodgkin's Lymphoma, Protocol CCBX001-049
McCune DE #205093	O	M	A Phase 3, Double-Blind, Placebo-Controlled Study of Maintenance Premetrexed plus Best Supportive Care versus Best Supportive Care Immediately Following Induction Treatment for Advanced Non-Small Cell Lung Cancer AND COMPANION STUDY Companion Translational Research Protocol
McCune DE #206014	O	M	A Phase I/II Trial of Zometa in Patients with Monoclonal Gammopathy of Undetermined Significance (MGUS)
McCune DE #205016	T	M	A Phase II Multicenter, Randomized, Double-blind, Placebo-controlled Dose-Ranging, Parallel Group Study of the Safety and Efficacy of the Oral Neurokinin-1 Receptor Antagonist, GW679769, When Administered as 50mg, 100mg, and 150mg Oral Tablets in Combination with Ondansetron Hydrochloride and Dexamethasone for the Prevention of Chemotherapy-Induced Nausea and Vomiting in Cancer Subjects Receiving Moderately Emetogenic Chemotherapy
McCune DE #205087	S	M	A Phase II, Open Label, Multi-center Study of EP2101 Therapeutic Vaccine in Patients with Stage IIb, Stage IV, or Recurrent Non-Small Cell Lung Cancer (NSCLC)
McCune DE #205070	O	M	A Phase II Study Using Alemtuzumab Combined with Fludarabine for the Treatment of Relapsed/Refractory B-cell Chronic Lymphocytic Leukemia (B-CLL)

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McCune DE #206126	O	L	A Phase II Trial of Imatinib (Gleevec) Plus Gemcitabine In Patients With Ovarian Carcinoma Who Have Failed At Least One Prior Chemotherapy
McCune DE #204114	O	M	A Phase II Trial of Weekly Docetaxel plus Every 3-Week Carboplatin in Patients with Stage IIIB/IV Non-small Cell Lung Cancer, Protocol GIA 12156
McCune DE #204006	T	M	A Phase III, Randomized, Double-blinded Efficacy and Safety Study of Three Doses of TAS-108 Administrated Orally in Postmenopausal Patients with Locally Advanced or Locally Recurrent Inoperable or Progressive Metastatic Breast Carcinoma Following Standard First Line Endocrine Therapy, Protocol Number TAS108-0004
McCune DE #204044	O	M	A Phase III Study of Delayed vs. Immediate Second-line Therapy with Docetaxel after Gemcitabine + Carboplatin in Advanced Non-Small Cell Lung Cancer, Protocol Number B9E-US-S245
McCune DE #204096	C	M	A Randomized, Open-Label Study of PROCRT® (Epoetin Alfa) Initiated at 40,000 Units Every Week Versus 80,000 Units Every Two Weeks In Anemic Patients With Cancer Receiving Chemotherapy, Protocol PR03-27-064
McCune DE #202083	O	M	A Randomized Phase III Trial of Gemzar versus Doxil with Crossover Treatment Option for Patients with Platinum-Resistant Ovarian, Fallopian Tube or Primary Peritoneal Cancer Undergoing Second or Third-Line Chemotherapy, Protocol Number: B9E-US-S301
McCune DE #204107	S	S	CTSU ACOSOG-Z9001, A Phase III Randomized Double-blind Study of Adjuvant STI571 (Gleevec™) Versus Placebo in Patients Following the Resection of Primary Gastrointestinal Stromal Tumor (GIST)
McCune DE #202114	O	S	CTSU CALGB 40101, Cyclophosphamide and Doxorubicin (CA) (4 VS 6 Cycles) versus Paclitaxel (4 VS 6 Cycles) as Adjuvant Therapy for Women with 0-3 Positive Axillary Lymph Nodes: A 2X2 Factorial Phase III Randomized Study
McCune DE #202089	O	S	CTSU CALGB 49907, A Randomized Trial of Adjuvant Chemotherapy With Standard Regimens, Cyclophosphamide, Methotrexate and Fluorouracil - (CMF) or Doxorubicin and Cyclophosphamide - (AC), Versus Capecitabine in Women 65 Years and Older with Node Positive or Node Negative Breast Cancer
McCune DE #204124	C	S	CTSU CALGB 80303, A Randomized Phase III Trial of Gemcitabine plus Bevacizumab (NSC #704865 IND #7921) Versus Gemcitabine plus Placebo in Patients With Advanced Pancreatic Cancer
McCune DE #202088	O	S	CTSU E1A00 A Randomized Phase III Trial of Thalidomide (NSC #66847) Plus Dexamethasone versus Dexamethasone in Newly Diagnosed Multiple Myeloma
McCune DE #204072	C	S	CTSU E3201 Intergroup Randomized Phase III Study of Postoperative Irinotecan, 5-Fluorouracil and Leucovorin vs Oxaliplatin, 5-Fluorouracil and Leucovorin vs 5-Fluorouracil and Leucovorin for Patients with Stage II or III Rectal Cancer Receiving Either Preoperative Radiation and 5-Fluorouracil or Postoperative Radiation and 5-Fluorouracil

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McCune DE #204043	O	S	CTSU IBCSG Trial 25-02, Tamoxifen and Exemestane Trial (TEXT), A Phase III Trial Evaluating the Role of Exemestane Plus GnRH Analogue as Adjuvant Therapy for Premenopausal Women with Endocrine Responsive Breast Cancer
McCune DE #204035	O	S	CTSU NCIC CTG MA.27, A Randomized Phase III Trial of Exemestane Versus Anastrozole in Postmenopausal Women With Receptor Positive Primary Breast Cancer
McCune DE #205071	T	S	CTSU NSABP 80101 Phase III Intergroup Trial of Adjuvant Chemoradiation after Resection of Gastric or Gastroesophageal Adenocarcinoma
McCune DE #202043	O	S	CTSU RTOG 98-04: Phase III Trial of Observation +/- Tamoxifen vs. RT +/- Tamoxifen for Good Risk Duct Carcinoma In-Situ (DCIS) of the Female Breast
McCune DE #206112	O	G	CTSU/GOG 0218 A Phase III Trial of Carboplatin and Paclitaxel Plus Placebo Versus Carboplatin and Paclitaxel Plus Concurrent Bevacizumab (NSC #704865, IND #7921) Followed By Placebo, Versus Carboplatin and Paclitaxel Plus Concurrent and Extended Bevacizumab, In Women With Newly Diagnosed, Previously Untreated, Suboptimal Advanced Stage Epithelial Ovarian and Primary Peritoneal Cancer
McCune DE #206054	O	M	NSABP B-38 A Phase III Adjuvant Trial Comparing Three Chemotherapy Regimens in Women with Node-Positive Breast Cancer: Docetaxel/Doxorubicin/Cyclophosphamide (TAC); Dose-Dense (DD) Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel (DD AC-P); DD Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel Plus Gemcitabine (DD AC-PG)
McCune DE #206073	O	M	Phase 1/2 study of ZK-Epothilone (ZK-Epo; ZK 219477) in combination with carboplatin in patients with platinum-sensitive, recurrent ovarian cancer
McCune DE #204008	O	M	Phase II Trial of ONTAK® in Refractory or Relapsed Advanced Non-small Cell Lung Cancer (NSCLC)
McCune DE #206084	O	M	Pilot Study to Evaluate the Safety and Efficacy of PROCRIT (Epoetin alfa) 80,000 Units Once Every Four Weeks (Q4W) vs. 40,000 Units Once Every Two Weeks (Q2W) in Cancer Patients with Non-Chemotherapy Anemia
McCune DE #204080	O	M	Protocol U2963n: The National Lymphocare Study: An Observational Study of Treatment, Outcomes, and Prognosis in Patients With Follicular Non-Hodgkin's Lymphoma
McCune DE #202107	C	L	Randomized Study of Docetaxel Versus Docetaxel Plus Genasense™ (G3139; Bcl-2 Antisense Oligonucleotide) in Patients with Previously Treated Non-Small Cell Lung Cancer, No. N304
McCune DE #206055	O	S	SWOG S0424: Molecular Epidemiology Case-Series Study of Non-Small Cell Lung Cancer in Smoking and Non-Smoking Women and Men
McCune DE #206013	O	S	SWOG S0435 A Phase II Trial of BAY 43-9006 (SNC-724772) in Patients with Platinum-Treated Extensive Stage Small Cell Lung Cancer

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Mysliwiec AG #205036	O S	CTSU NSABP C-08, A Phase III Clinical Trial Comparing Infusional 5-Fluorouracil (5-FU), Leucovorin, And Oxaliplatin (mFOLFOX6) Every Two Weeks With Bevacizumab To The Same Regimen Without Bevacizumab For The Treatment Of Patients With Resected Stages II And III Carcinoma of the Colon
Mysliwiec AG #206025	T M	RegistHER: An Observational Cohort Study of Patients with HER2-Positive Metastatic Breast Cancer
Ramsdell MJ #204082	O L	Evaluating Cognitive Function in Women Receiving Chemotherapy for Newly Diagnosed Breast Cancer

**INTERNAL MEDICINE SERVICE, DEPARTMENT OF MEDICINE**

Avalos C #205046	O L	The Effect of Blood Transfusion on Serum Ferritin and Iron
Bauler KC #205123	O L	Current Use and Complications of Peripherally Inserted Central Catheters (PICC): A Retrospective Study
DeHaan PJ #205039	O L	Management of Parapneumonic Effusions: Does Following Pneumonia Treatment Guidelines Affect Outcome? A Retrospective Study
Evans NR #206119	O L	Urinary Markers of Renal Injury and N-Acetylcysteine Efficacy (URINE)
Fischer CJ #206064	C L	Does Participation in a Subspecialty Elective Rotation Improve the Respective American Board of Internal Medicine Subspecialty Score?
Kiley CA #205104	C L	Appropriate Use of CTPA in the Evaluation of Pulmonary Embolism - An Examination of Hospital-Wide Referral Practices
Kwon HP #206087	O L	Hemoptysis in Young Adults
Kwon HP #206069	O L	The Effects of Nighttime Low Dose Aspirin on Ambulatory Blood Pressure Testing in Treated Hypertensive Patients
Mount GR #205038	T L	Effect of A Single Intra-articular Steroid Injection on Serum Fructosamine Levels in Patients with Type 2 Diabetes Mellitus
Short PA #202048	O M	A Multinational, Randomized, Double-blind, Placebo-controlled, Forced-titration, 2X2 Factorial Design Study of the Efficacy and Safety of Long Term Administration of Nateglinide and Valsartan in the Prevention of Diabetes and Cardiovascular Outcomes in Subjects with Impaired Glucose Tolerance (IGT), Protocol No. CDJN608 B2302
Short PA #204045	O M	A Prospective, multinational, multicenter, double-blind, randomized, active-controlled trial to compare the effects of Lotrel (amlodipine/benazepril) to benazepril and hydrochlorothiazide combined on the reduction of cardiovascular morbidity and mortality in patients with high risk hypertension, Protocol No. CCIB002I2301: ACCOMPLISH (Avoiding Cardiovascular Events through COMbination Therapy in Patients Living with Systolic Hypertension)
Wang JY #205004	C L	Efficacy of Iron in Restless Legs Syndrome (RLS) Patients With Low-Normal Ferritin: A Randomized, Double-Blind, Placebo Controlled Study

**NEPHROLOGY SERVICE, DEPARTMENT OF MEDICINE**

Lee JY #205121	C L	Does High Resistive Index by Doppler Ultrasonography Predict Small Kidney Sizes?
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**NEUROLOGY SERVICE, DEPARTMENT OF MEDICINE**

Erickson JC #204062	O L	A Randomized Trial of a Migraine Management Seminar in the Treatment of Migraines
Erickson JC #203048	O L	A Randomized Trial of B Vitamins for Alzheimer's Disease
Erickson JC #206075	O L	Association Between Migraine and Psychiatric Conditions In Soldiers Returning from Combat
Erickson JC #203097	O M	CLOSURE I Trial: A Prospective, Multicenter, Randomized, Controlled Trial to Evaluate the Safety and Efficacy of the STARFlex Septal Closure System Versus Best Medical Therapy in Patients with a Stroke and/or Transient Ischemic Attack Due to a Presumed Paradoxical Embolism Through a Patent Foramen Ovale
Erickson JC #205107	C L	Diagnosis and Treatment of Migraines in U.S. Army Soldiers
Erickson JC #205118	O L	Prevalence and Impact of Migraine Among Deployed Soldiers
Erickson JC #205115	O M	Study of Acute Viprinex™ for Emergency Stroke: A Randomized, Double-Blind, Placebo-Controlled Study of Viprinex™ (Ancrod Injection) in Subjects Beginning Treatment within 6 Hours of the Onset of Acute, Ischemic Stroke

**PULMONARY DISEASE & CRITICAL CARE SERVICE, DEPARTMENT OF MEDICINE**

Caras WE #205032	T L	Adjunctive Role of Mirtazapine in Mild Positional Sleep Apnea
Clagett CL #206083	T M	A Randomized, Double-blind, Placebo-controlled, Parallel Group, Stratified, Multi-center, 12 Week Study Comparing the Safety and Efficacy of Fluticasone and Formoterol Combination (FlutiForm™ 100/10 mcg twice daily) in a Single Inhaler (SkyePharma HFA pMDI) with the Administration of Placebo or Fluticasone (100 mcg twice daily) and Formoterol (10 mcg twice daily) Alone in Adolescent and Adult Patients with Mild to Moderate Asthma
Mysliwiec V #206086	O L	Identifying Adherence Obstacles to CPAP Therapy
Niven AS #205128	O L	Impulse Oscillometry and Obstructive Lung Disease: Assessment of a Clinically Significant Bronchodilator Response

**NUTRITION CARE DIVISION**

Cates-Gorang CC #206008	O L	Attenuation of Exertional Muscle Damage with a Nutritional Supplement
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**DEPARTMENT OF NURSING**

DePew CL #206093	O L	Effects on Aspirated Volume, Patency, and Tracheal Mucosa using High Intermittent Negative Pressure versus Low Continuous Negative Pressure for Subglottic Secretion Aspiration
Jones JM #203030	C L	Junior Army Nurse Corps Officers' Perceptions, Experiences and Expectations of Head Nurse Leadership
Loan LA #205117	O L	A Qualitative Descriptive Study that Identifies Essential Competencies and Leadership Characteristics of Army Adult Medical-Surgical Critical Care Head Nurses (dissertation)
Loan LA #202066	O L	Caring Interventions for Couples Who Have Miscarried



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Loan LA #205037	O L	Determining the Effectiveness of a Stroke Prevention Program
Loan LA #204084	O L	Impact of Inpatient Physician Order Entry on Medication Administration and Dispensing Error Rates in the Neonatal Intensive and Intermediate Care Units
Loan LA #204031	O M	Military Nursing Outcomes Database: Analysis & Expansion (MilNOD IV)
Loan LA #201104	O L	Newborn Infant Speech Perception
Loan LA #202075	O L	Secondary Analysis of NICU Modified Care Environment Projects
McNabb LA #206108	O L	Army Nurse Corps Officers' Deployment Experiences and Reintegration
Trego LL #206107	O L	Menstruation During Deployment: Women's Attitudes Towards Menstrual Suppression
Trego LL #206002	C L	Military Women's Thoughts about Menstruation and Menstrual Suppression During Deployment

**ANESTHESIA STUDENTS, DEPARTMENT OF NURSING**

Hannon MK #204112	C L	Efficacy of Preoperative Valerian (Night Before) on Day of Surgery Anxiety
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**DEPARTMENT OF OBSTETRICS/GYNECOLOGY**

Burris AC #206042	C L	Resident Training in Assessment of the Sexual Assault Patient Utilizing Simulation
Chinn MK #205140	O L	Continuous Use of the Oral Contraceptive for Menstrual Cycle Suppression and the Effects on Bone Density; a Prospective, Randomized, Clinical Trial
Dainty LA #81035	O G	GOG 0041: Surgical Staging of Ovarian Carcinoma
Dainty LA #81105	O G	GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma
Dainty LA #84033	O G	GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease
Dainty LA #84074	O G	GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements
Dainty LA #86089	O G	GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes
Dainty LA #87104	O G	GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy

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Dainty LA #87028	O	G	GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAi and IBi and IAii and IBii Ovarian Cancer, Phase III
Dainty LA #87091	O	G	GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma
Dainty LA #93063	O	G	GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix
Deering SH #206029	O	L	Simulation Training for Postpartum Hemorrhage
Flood SK #206098	O	L	Serum Estradiol Levels in Patients with Polycystic Ovarian Syndrome undergoing Ovulation Induction with Clomiphene Citrate
Han JJ #99077	C	L	Misoprostol for the Medical Management of Non-viable First Trimester Pregnancies
Hill DL #204111	O	M	Glyburide Compared to Insulin in the Management of White's Classification A2 Gestational Diabetes
Hill DL #206099	O	L	Molecular mechanisms of progesterone mediated inhibition of LPS and other inflammatory agent induced production of pro-inflammatory cytokines in the fetal-maternal circuitry of the human placenta
Howard BC #203067	O	L	The Effects of IL-10 on the Production of Inflammatory Cytokines in a Placental Artery Explant Model
Howard BC #203066	O	L	The Production of Immunoregulatory Cytokines in a Placental Artery Explant Model
Howard BC #204088	O	M	Use of Transvaginal Cervical Length Measurements in Twin Gestations
Lattu AL #205005	O	L	The Distribution of Bishop Scores and Quantitative Values of Fetal Fibronectin (fFN) in Nulliparous Patients Between 37-42 Weeks Gestation: A Prospective Observational Study
Lattu AL #203078	O	L	Use of Pipelle Endometrial Sampling in the Evaluation of Abnormal First Trimester Pregnancy
Manshande MM #205089	O	L	Pilot Study of a Novel Cord Blood Collection Technique
Napolitano PG #203045	O	M	Randomized Controlled Trial of Endurance Exercise and Gallbladder Disease Risk in Overweight Pregnant Women
Napolitano PG #203001	O	B	The Effect of Magnesium on Matrix Metalloproteinase-9 Activity in Umbilical Cord Blood at Delivery of Pregnancies Complicated by Chorioamnionitis
Napolitano PG #203099	O	L	Umbilical Cord Plasma Homocysteine Concentrations at Delivery in Pregnancies Complicated by Preeclampsia
Paonessa DJ #204108	C	L	The Effects of Cholic Acid and Deoxycholic Acid on Placental Artery Perfusion Pressures in the Ex Vivo Placental Cotyledon Model
Zalucki CM #205021	O	L	Correlation of Persistent Anal Sphincter Defects and Symptoms following Repair of Anal Sphincter Lacerations due to Obstetric Injury in Primiparous Women

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**DEPARTMENT OF PATHOLOGY**

Ager EP #203095	T M	Implementation of the SARS Coronavirus Real-Time PCR Primers and Probes Assay to Detect SARS Coronavirus in Respiratory Specimens
Ager EP #203041	O M	Use of a Non-FDA Approved Gene Amplification Test To Detect or Rule-Out Vaccinia in Patients With Complications Following Smallpox Vaccination or Possible Contact Vaccinia
Andrews JM #205102	O L	Absolute Lymphocytosis in Adults: A Laboratory Protocol
Champeaux AL #205042	O L	Incidental Anatomic and Histologic Findings in Bariatric Surgery Specimens

**DEPARTMENT OF PEDIATRICS**

Cason RL #203014	T L	Clinical Use of Reticulocyte Hemoglobin to Detect Iron Deficiency at the 12 Month Well Baby Visit
Davis BE #204104	O M	Health, Quality of Life & Activity in Cerebral Palsy
Davis BE #204074	O M	Survey of Chronic Pain and Its Effects on Youth With Disabilities
Ervin MK #206049	O L	An Observational Study to Determine the Factors Influencing Bone Mineral Density in Post-Menarchal Adolescents with Neuromuscular Disabilities
Fairchok MP #205138	O M	Evaluation of Serologic Responses to Fluzone® in Infants > 6 Months of Age Who Did or Did Not Receive Fluzone Vaccine at 2 Months of Age
Fairchok MP #203052	C M	Improving the Delivery of Influenza Vaccine to Young Children: A Comparison of Two Influenza Vaccine Regimens
Fairchok MP #205137	T M	Safety and Immunogenicity of Fluzone® Influenza Virus Vaccine (2005-2006 Formulation) Among Healthy Children 6 to 12 Weeks of Age
Fairchok MP #205034	C M	Safety and Immunogenicity of Influenza Virus Vaccine Fluzone® 2004-2005 Among Healthy Children 2 Months vs 6 Months of Age
Fairchok MP #205139	O L	The Impact of Human Metapneumovirus Versus other Common Respiratory Viruses in Infants in Fulltime Daycare
Fitzgerald KL #206035	O M	Military Children at Risk - Enhancing Quality of Life (mCARE) Needs Assessment
Gries DM #205065	O L	Staphylococcus Aureus Intestinal Colonization Among Healthy Infants
Harsha WT #204097	T A	Effect of Immunomodulatory Diet Upon 5-Fluorouracil Induced Oral and Intestinal Mucositis in Golden Syrian Hamsters (Mesocricetus auratus)
Johnson ER #206021	O L	EKG Screening in ROTC Cadets; Is It Useful?
Kramer LC #203119	O L	Alternating Antipyretics: Antipyretic Efficacy Of Acetaminophen Versus Acetaminophen Alternated With Ibuprofen In Children
Lieuw KH #205110	O C	AALL03N1, Understanding the Ethnic and Racial Differences in Survival in Children with Acute Lymphoblastic Leukemia

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Lieuw KH #206052	O	C	ACNS0331 A Study Evaluating Limited Target Volume Boost Irradiation and Reduced Dose Craniospinal Radiotherapy (18.00 Gy) and Chemotherapy in Children with Newly Diagnosed Standard Risk Medulloblastoma: A Phase III Double Randomized Trial
Lieuw KH #206095	O	C	AEWS02B1, A Group wide Biology and Banking Study for Ewing Sarcoma
Lieuw KH #206096	O	C	AHOD0431, A Phase III Study for the Treatment of Children and Adolescents with Newly Diagnosed Low Risk Hodgkin Disease
Lieuw KH #206051	O	M	ANBL0032 Phase III Randomized Study Of Chimeric Antibody 14.18 (Ch14.18) In High Risk Neuroblastoma Following Myeloablative Therapy And Autologous Stem Cell Rescue
Lieuw KH #206097	O	C	AREN03B2; Renal Tumors Classification, Biology, and Banking Study
Lieuw KH #200032	C	C	COG 9900, ALinC 17, Classification (C), B-Precursor Induction Treatment (I) Protocol
Lieuw KH #200077	O	C	COG 9904, ALinC 17: Treatment for Patients with Low Risk Acute Lymphoblastic Leukemia, A Phase III Study
Lieuw KH #200139	O	C	COG A5971: Randomized Phase III Study for the Treatment of Newly Diagnosed Disseminated Lymphoblastic Lymphoma or Localized Lymphoblastic Lymphoma, A Phase III COG Study
Lieuw KH #205015	O	C	COG AALL0031, A COG Pilot Study for the Treatment of Very High Risk Acute Lymphoblastic Leukemia in Children and Adolescents
Lieuw KH #205068	O	C	COG AALL0232, High Risk B-precursor Acute Lymphoblastic Leukemia
Lieuw KH #205095	O	C	COG AALL0331, Standard Risk B-precursor Acute Lymphoblastic Leukemia; A Phase III Group-Wide Study
Lieuw KH #205067	O	C	COG AALL03B1, Classification of Acute Lymphoblastic Leukemia
Lieuw KH #205026	C	C	COG AAML03P1, Treatment of Newly Diagnosed Childhood Acute Myeloid Leukemia (AML) Using Intensive MRC-Based Therapy and Gemtuzumab Ozogamicin (GMTZ): A COG Pilot Study
Lieuw KH #205122	C	C	COG ACNS0126, A Phase II Study of Temozolomide in the Treatment of Children with High-grade Glioma or diffuse intrinsic Pontine Gliomas
Lieuw KH #206034	O	C	COG ACNS0423: A Phase II Study of Concurrent Radiation and Temozolomide Followed by Temozolomide and Lomustine (CCNU) in the Treatment of Children with High Grade Glioma
Lieuw KH #205084	O	C	COG AGCT0132, A Phase III Study of Reduced Therapy in the Treatment of Children with Low and Intermediate Risk Extracranial Germ Cell Tumors
Lieuw KH #203024	O	C	COG AHOD0031, A Phase III Group-wide Study of Dose-intensive Response-based Chemotherapy and Radiation Therapy for Children and Adolescents with Newly Diagnosed Intermediate Risk Hodgkin Disease
Lieuw KH #205047	C	C	COG AHOD00P1, A Pilot Study of Re-Induction Chemotherapy with Ifosfamide, and Vinorelbine (IV) in Children with Refractory/Relapsed Hodgkin Disease

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Lieuw KH #205014	O	C	COG AHOD0321, A Phase II Study of Weekly Gemcitabine and Vinorelbine in Children with Recurrent or Refractory Hodgkin Disease
Lieuw KH #201108	O	C	COG ANBL00B1, Neuroblastoma Biology Studies
Lieuw KH #205069	C	C	COG ANHL0121, A Phase II Study of Rituximab (IND#7028) and Ifosfamide, Carboplatin and Etoposide (ICE) Chemotherapy in Children with Recurrent/Refractory B-cell (CD20+) Non-Hodgkin Lymphoma and B-cell Acute Lymphoblastic Leukemia
Lieuw KH #200049	O	C	COG D9902, A COG Soft Tissue Sarcoma Diagnosis, Biology and Banking Protocol
Lieuw KH #98090	O	C	COG P9442: National Wilms Tumor Late Effects Study
Lieuw KH #201054	C	C	COG P9934: Systemic Chemotherapy, Second Look Surgery and Conformal Radiation Therapy Limited to the Posterior Fossa and Primary Site for Children > 8 Months and < 3 Years with Non-metastatic Medulloblastoma - A Children's Oncology Group Phase III Study
Lieuw KH #205105	O	C	COG-LTF, A Groupwide Process for Collecting Long Term Follow Up Data
Lieuw KH #94092	O	C	POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma
Lieuw KH #95058	C	C	POG 9400: ALinC 16 Classification (C) Protocol
Lieuw KH #96097	O	C	POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study
Lieuw KH #200018	C	C	POG P9761: Phase II Trial of Irinotecan in Children with Refractory Solid Tumors: A COG Study
Lieuw KH #200048	O	C	POG P9851: Osteosarcoma Biology Protocol, Companion to Group-Wide Therapeutic Studies
Lieuw KH #203105	C	C	POG P9962 A Phase II Study of Intrathecal Topotecan in Patients with Refractory Meningeal Malignancies
Maranich AM #206045	C	L	The Pontine Valentine Leucocidin Virulence Factor in Staph Aureus Disease: A Retrospective Study Analyzing CA-MRSA Incidence and Clinical Severity
Moffitt DR #204040	O	M	National Cystic Fibrosis Foundation Patient Data Registry
Puntel RA #204028	O	A	Pediatric Intubation Training Utilizing the Ferret (mustela putorius furo) Model
Puntel RA #203046	O	M	Telemedicine Based Ultrasound for Detecting Neonatal Heart Disease in Babies at Remote Military or Native American Health Care Facilities

#### **DEPARTMENT OF PHARMACY**

Booth HS #206092	C	L	Assessment of LDL-Cholesterol Goal Attainment Among Patients at a Very High Risk For Secondary Cardiovascular Events in a Pharmacist-Managed Lipid Clinic
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**Prin. Invest.**  
**#Protocol No.**

**S T Title**

**DEPARTMENT OF PREVENTIVE MEDICINE**

Hoang HV #206056	C L	Will Power: Is Personal Motivation Associated with Retention in the Army?
Hughes VR #206066	C L	Self Identification as a Predictor of Subsequent Mental Health Diagnosis
Moore CA #206074	C L	Military Rank as a Risk Factor for Type 2 Diabetes in Military Spouses
Ross TW #206033	C L	Hazards to Hearing and Threshold Shifts: The Results of Deployment to a Combat Environment
Wiesen AR #205099	O L	CD4+ T Cell Epitope Identification for Protective Antigen of Bacillus Anthracis

**DEPARTMENT OF PSYCHIATRY**

Peterson KA #204089	O M	A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced Nightmares and Sleep Disturbance
Peterson KA #206011	O M	Prazosin for the Treatment of Trauma Nightmares in PTSD

**DEPARTMENT OF PSYCHOLOGY**

Darnell JN #206062	O L	Military Readiness Risks: Leader Perspectives Impact on Mandatory Addiction Referrals
Johnson PL #205019	O L	Theory-Guided Anticipatory Guidance
Lucenko BA #206088	O L	Exposure to Death and Dying and Mental Health Response in Operation Iraqi
Reger GM #206118	O L	User Centered Design Feedback for the Virtual Iraq
Reger MA #206077	O L	Army Suicide Event Report: Data Analysis

**DEPARTMENT OF RADIOLOGY**

Balingit AG #202117	O L	Intravenous Administration of 131 I-6-B Iodomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging
Reece WB #206053	O M	NSABP B-39 / RTOG 0413 A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I or II Breast Cancer
Reece WB #204069	O S	SWOG RTOG 0212, A Phase II/III Randomized Trial of Two Doses (Phase III-Standard vs. High) and Two High Dose Schedules (Phase II-Once vs Twice Daily) for Delivering Prophylactic Cranial Irradiation for Patients With Limited Disease Small Cell Lung Cancer
Semerad DC #205134	O L	Clinical Trial and Retrospective Review to Determine the Sensitivity and Specificity of Iminodiacetic Acid Scintigraphy for Fibrolamellar Carcinoma
Statler JD #205051	O L	Carotid Stenosis: Digital Subtraction Angiography, Magnetic Resonance Angiography, and the Evolution of Preoperative Evaluation
Statler JD #205024	O L	Computed Tomography of the Abdomen Following Appendectomy

**Prin. Invest.**  
**#Protocol No.**

**S T Title**

**SPECIAL FORCES GROUP, FORT LEWIS**

Wendt EP #206106 O A 1st Special Forces Group (Airborne) Combat Trauma Management Procedures Training for Special Forces Medical Personnel

Wendt EP #206018 O A 1st Special Forces Group (Airborne) Instructing Combat Trauma Management to Trainees

**GENERAL SURGERY SERVICE, DEPARTMENT OF SURGERY**

Arthurs ZM #206032 O L Colonic Ischemia Following Abdominal Aortic Aneurysm Repair-- Open vs. Endovascular Approaches

Arthurs ZM #206123 O L Renovascular Hypertension: A Retrospective Analysis of Renal Artery Stenting Outcomes

Arthurs ZM #203090 O L The Association Of Elevated C-Reactive Protein With Presence And Degree Of Carotid Stenosis

Azarow KS #203107 C M A Multicenter, Open-Label, Randomized Study To Compare The Safety And Efficacy Of Once Daily Levofloxacin Along With Once Daily Metronidazole Versus Piperacillin / Tazobactam In The Treatment Of Complicated Appendicitis, Protocol CAPSS-151

Azarow KS #204013 C L Abdominal Wall Defects: Does the Intraabdominal Pressure Affect Outcome?

Beekley AC #204058 O A Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/Capra hircus, Pig/Sus scrofa)

Beekley AC #205075 O L Operation Iraqi Freedom Combat Trauma Database from the 31st Combat Support Hospital, Baghdad, Iraq

Brown TA #204106 C M A Multicenter, Double-blind, Randomized, Phase 3 Study to Compare the Safety and Efficacy of Intravenous Doripenem with that of Meropenem in Complicated Intra-abdominal Infections

Brown TA #206015 O M A Prospective Randomized Study Comparing Sentinel Lymph Node (SLN) Evaluation with Standard Pathological Evaluation for the Staging of Colon Carcinoma

Brown TA #205074 C M A Randomized, Double-Blind Study of GT267-004 Versus Vancomycin, and GT267-004 Versus Metronidazole, in Patients with C.Difficile-Associated Diarrhea; Protocol GD3-170-301

Brown TA #205096 C M ACOSOG Z4031, Use of Proteomic Analysis of Serum Samples for Detection of Non-Small Cell Lung Cancer

Brown TA #206101 O M ACOSOG Z6041: A Phase II Trial of Neoadjuvant Chemoradiation and Local Excision for uT2uN0 Rectal Cancer

Brown TA #205098 T M ACOSOG Z9031, A Phase III Randomized Study of Preoperative Radiation Plus Surgery Versus Surgery Alone for Patients with Retroperitoneal Sarcomas (RPS)

Brown TA #205097 T M Biological Relevance of Sentinel Lymph Node (SLN) Micrometastasis in Patients With Colon Carcinoma

Brown TA #203077 E A Comparative Medical/Surgical Research and Development (Limited)

Brown TA #206110 O A Comparative Medical/Surgical Research and Development (Limited)

Brown TA #205112 O S RTOG 0412 / SWOG S0332, Phase III Randomized Trial of Preoperative Chemotherapy Versus Preoperative Concurrent Chemotherapy and Thoracic Radiotherapy Followed By Surgical Resection and Consolidation Chemotherapy in Favorable Prognosis Patients with Stage IIIA (N2) Non-Small Cell Lung Cancer

<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b><u>Title</u></b>
Brown TA #205113	C	S	SWOG 9430, A Phase II Trial of Complete Surgical Resection for Stage IV Melanoma - Surgical Resection With Biological Evaluation And Clinical Follow-Up
Brown TA #205114	C	S	SWOG 9431, Cytogenetic Molecular and Cellular Biology Studies in Metastatic Melanoma Patients, Ancillary
Carter PL #202013	O	L	Bariatric Surgery Effects on the Comorbidities of Obesity
Cronk DR #204001	O	L	Does Intestinal Fatty Acid Binding Protein Predict Strangulation in Mechanical Small Bowel Obstruction?
Cronk DR #206040	O	L	Does SDF-1 Production by Atherosclerotic Plaques Correlate with Severity of Carotid Artery Stenosis?
Cuadrado DG #206041	O	L	Breast Abscesses Following Nipple Piercing: A Case Series and Review of the Literature
Cuadrado DG #203114	C	L	Chewing Gum for the Reduction of Postoperative Ileus After Elective Open Colectomy
Cuadrado DG #206016	T	L	Determining the Incidence of Sonographically Detectable Wound Seromas in the Morbidly Obese: A Pilot Study
Cuadrado DG #203034	O	L	Impact of Gastric Bypass with Subtotal Gastrectomy on Plasma Ghrelin Profile
Eckert MJ #206047	C	L	Bronchoscopy in the Blast Injury Patient
Eckert MJ #206115	O	A	Hypoxemic Reperfusion Following Lower Torso Ischemia in sp. Sus scrofa
Eckert MJ #205080	O	A	Stem cell engraftment in the lipopolysaccharide mouse (Mus musculus) model of acute inflammatory injury
Eggebroten WE #204101	T	A	Advanced Trauma Life Support (ATLS) Training Utilizing the Goat (Capra hircus)
Hartenstine MJ #204100	O	L	Human Blood Collection for Bench Research Initiatives
Herbert GS #206026	O	L	Determination of Telomerase Activity in Atypical Ductal Hyperplasia of the Breast
Herbert GS #206010	O	L	Does Control of Inflammation Prior to Intervention for Carotid Artery Disease or Lower Extremity Peripheral Arterial Disease Affect Outcome?
Herbert GS #201020	O	L	Learning Curves for Airway Assessment and Endotracheal Intubation - Cumulative Sum Analysis
Herbert GS #206027	O	L	Prognostic Significance of Telomerase Activity in T1 and T2 Rectal Adenocarcinoma for Patients Undergoing Transanal Excision
Herbert GS #205125	O	L	Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Delayed Gastric Emptying after Pancreaticoduodenectomy
Herbert GS #205126	O	L	Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Post-Operative Ileus Following Partial Colectomy
Herbert GS #205063	O	L	The Impact of Nodal Micrometastases on Survival of Women with Breast Cancer
Husain FA #202073	T	M	Ultrasound Imaging for Central Venous Catheter Placement in the Intensive Care Unit: Is Real-time Really Better? A Prospective Randomized Trial



<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b><u>Title</u></b>
Kjorstad RJ #206043	O	L	Colorectal Complications of External Beam Radiation vs. Brachytherapy for Prostate Cancer
Kjorstad RJ #205127	T	L	Screening for Occult Vascular Injuries Utilizing a Portable Ultrasound Unit
Martin MJ #206079	O	L	The Utility and Impact of Standard Trauma Triage Criteria in the Elderly
Mullenix PS #203091	T	L	Prospective Evaluation Of Intraoperative Duplex Ultrasound As An Adjunct To Technical Excellence During Carotid Endarterectomy
Perry JT #206061	O	L	Utilization of Genetic Testing and Counseling Among Patients with Hereditary Non-Polyposis Colorectal Cancer
Perry JT #206038	O	L	Venous Distensibility Index as a Predictor of Radiocephalic Arteriovenous Fistula Maturation
Sohn VY #206116	O	L	Breast Papillomas in the Era of Stereotactic Core Biopsy
Sohn VY #206114	O	L	Institutional Accuracy of 11- and 8- Gauge Vacuum-Assisted Core Biopsy of Mammographic Breast Lesions
Sohn VY #206004	O	A	The Evaluation of Telomerase Inhibition in a Colorectal Metastasis Model Using Nude Mice (Mus musculus)

#### **OPHTHALMOLOGY SERVICE, DEPARTMENT OF SURGERY**

Ainbinder DJ #204085	C	L	Flow Cytometry Descriptive Findings from Lacrimal Sac Biopsy Specimens, Obtained in Standard Dacryocystorhinostomy
Boden JH #206076	C	L	Methicillin Resistant Ascending Facial and Orbital Cellulitis in Operation Iraqi Freedom Troop Population
Boden JH #206124	O	L	The use of lidocaine gel prior to povidone - iodine antisepsis and its effect on microbial survivability
Solverson DJ #206006	O	L	Virtual Ophthalmosurgical Simulator as a Valid Training Tool
Torres MF #204049	C	L	Long-Term Follow-up of Military Personnel Following Photorefractive Keratectomy With Mitomycin-C
Torres MF #205083	O	L	Ophthalmic Phentolamine Multiple Dose Clinical Trial

#### **ORTHOPEDICS SERVICE, DEPARTMENT OF SURGERY**

Antosh IJ #206022	O	L	Accuracy of Reduction Utilizing Volar Fixation for Dorsally Displaced Fractures of the Distal Radius
Arrington ED #206037	O	L	A Retrospective Review of Injuries Sustained During Operation Iraq Freedom and Operation Enduring Freedom Requiring Medical Evacuation to a Tertiary Medical Center
Arrington ED #201015	O	B	Biomechanics of Various Coracoclavicular Ligament Reconstruction Techniques
Arrington ED #204051	O	L	Efficacy of Post-operative Hip Spica Wrap Dressing after Primary Hip Arthroplasty in Preventing Post-operative Wound Complications and Blood Transfusions
Arrington ED #203036	O	L	Intramedullary Fixation of Displaced Acute Middle One-Third Clavicle Fractures
Arrington ED #206085	O	L	Pectoralis Major Repairs in Active Duty Soldiers
Arrington ED #206036	O	L	Return to Full Duty after Anterior Cruciate Ligament Reconstruction in the Military Population

<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b><u>Title</u></b>
Arrington ED #200065	C	M	Study of the Treatment of Articular Repair (STAR): A Prospective, Longitudinal Within Patient Evaluation of the Effectiveness (Durability) of Carticel (autologous cultured chondrocytes) Compared to Non-Carticel Surgical Treatment for Articular Cartilage Defects of the Knee
Arrington ED #200125	O	L	Subacromial Injection of Corticosteroids versus Ketoralac for Treatment of Shoulder Impingement Syndrome
Benfanti PL #205300	O	M	Stryker Biotech- OP-1 Bone Morphogenetic Protein, BMP-7 (HUD)
DeVine JG #205053	O	M	A Prospective, Randomized Clinical Investigation of the Cervitech, Inc. Porous Coated Motion Artificial Disc for Stabilization of the Cervical Spine at One Level between C3-C4 and C7-T1
DeVine JG #206120	O	M	A Single Blind, Multi-Center, Randomized, Prospective Clinical Study Comparing Optecure™ Autograft Extender to Autograft Only in Fusion of the Lumbar Spine
DeVine JG #206081	O	L	Magnetic resonance imaging evaluation of adjacent segments after lumbar disc arthroplasty using the SB Charite implant
Devine JG #206082	O	L	Magnetic Resonance Imaging Evaluation of Adjacent Segments After Cervical Disc Arthroplasty Using the PCM Implant
Driver VR #205054	C	M	A Phase 2, Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging Study to Evaluate the Efficacy and Safety of Three Doses of TAK-128 in Subjects with Mild to Moderate Diabetic Peripheral Neuropathy
Driver VR #204098	T	L	Cost of Treating Diabetic Foot Ulcers - At Madigan Army Medical Center
Ghidella SD #205013	O	M	A Double-blind, Randomized, Placebo-controlled Phase 2b Study to Establish the Effective Dose Range and to Evaluate the Safety of Chrysalin in Adult Subjects with a Fractured Distal Radius
Ghidella SD #206009	O	L	A Randomized Study of Volar Fixed-Angle Plate Fixation Versus Closed Management for Fractures of the Distal Radius
Ghidella SD #205079	O	A	Microsurgery Training Utilizing The Rat (rattus norvegicus) as a Teaching Model
Herzog JP #201112	C	L	Post-operative Shoulder Pain: A Prospective Randomized Trial Comparing the Pain Infusion Pump to the Pre-induction Interscalene Block
Schweinberger MH #202091	T	L	A Prospective, Randomized, Stratified, Parallel Group, Comparison Study of the Healing Rate of Chronic Neuropathic Ulcers Treated with Hyalofill versus Regranex

#### **OTOLARYNGOLOGY SERVICE, DEPARTMENT OF SURGERY**

Baumgartner BJ #204009	C	L	Evaluation of Dizziness / Vertigo by MRI/MRA: A Clinical Outcomes Study
Crawford JV #205052	O	M	MET™ Fully Implantable Ossicular Stimulator Clinical Trial Protocol
Crawford JV #204042	T	M	Rapid Employment of Acetylcysteine Treatment for Otologic Recovery (REACTOR), A Prospective, Multicenter, Randomized, Double-blind, Parallel, Placebo-controlled Study Assessing the Efficacy of the Nutritional Supplement N-Acetylcysteine Treatment of Acute Acoustic Trauma

<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b>Title</b>
Demars SM #206058	C	L	Effect of Smoking on Rate of Post-tonsillectomy Hemorrhage
Demars SM #206044	C	L	Review of Postoperative Complications after BAHA Implantation at Madigan AMC and Virginia Mason MC
Grafenberg MR #205050	O	L	Celecoxib Versus Oxycodone in Uvulopalatopharyngoplasty Surgery: A Comparison of Post-Operative Risks and Benefits
Grafenberg MR #205120	O	L	Complications and Audiologic/Tympanometric Findings in Children with Cleft Lip/Palate and Cleft Palate
Poss JM #206125	O	L	Base of Tongue Reduction for Persistent Obstructive Sleep Apnea Using the Coblator II System: A Pilot Study
Poss JM #206020	O	L	Clinical Survey of Community Physicians: Post-Tympanostomy Tube Placement and Swimming Precautions/Treatment Otitis Media with Effusion
Sorensen DM #203016	E	A	Pediatric Bronchoesophagology Laboratory Using Swine (Sus scrofa)
Sorensen DM #206030	O	A	Pediatric Bronchoesophagology Laboratory using Swine (Sus scrofa)
Sorensen DM #204070	O	L	Perioperative Immunonutrition in Head and Neck Cancer
Spear SA #206057	O	L	Review of Thyroid Cancer Treatment Outcomes at a Major Medical Center from 1996-2000
Thomas RF #205009	O	L	Inferior Turbinate Reduction Comparing Turbinate Microdebrider, Coblation and Bipolar Cautery

#### **UROLOGY SERVICE, DEPARTMENT OF SURGERY**

Baker KC #205129	T	M	A Multi-Center, Open-Label Evaluation of the Safety of Silodosin in the Treatment of the Signs and Symptoms of Benign Prostatic Hyperplasia, Protocol #SI040011
Baker KC #205092	O	M	A Multi-center, Randomized Clinical Investigation of Trelstar <sup>TM</sup> Versus Continued Therapy in Patients Receiving Lupron or Zoladex for Advanced Prostate Cancer
Baker KC #205072	C	M	A Multi-Center, Randomized, Double-Blind, Placebo Controlled, Parallel Evaluation of the Efficacy and Safety of Silodosin in the Treatment of the Signs and Symptoms of Benign Prostatic Hyperplasia, Protocol # SI04009
Baker KC #203035	O	M	A Multi-Institutional Pilot Study to Evaluate Molecular Markers in Urine and Serum in the Early Detection of Prostate Cancer
Baker KC #201113	O	M	A Phase III, Extension Study to Evaluate the Safety of 10 mg Atrasentan in Men with Hormone-Refractory Prostate Cancer (M00-258)
Baker KC #201107	O	M	A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer (M00-211)
Baker KC #201121	O	M	A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic, Hormone-Refractory Prostate Cancer (M00-244)
Baker KC #204005	O	M	A Phase III, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Ability of Risedronate to Prevent Skeletal Related Events in Patients with Metastatic Prostate Cancer Commencing Hormonal Therapy, Protocol #GU02-41

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Baker KC #204122	C	M	A Randomized, Double Blind, Placebo Controlled, Four Arm (Placebo, Tolterodine ER, Tamsulosin, and Tolterodine ER plus Tamsulosin) Study to Evaluate the Clinical Efficacy and Safety of Tolterodine ER 4 mg in Men who have Frequency and Urgency, with or without Urinary Urge Incontinence, with or without Bladder Outlet Obstruction, Protocol Number A6121120
Baker KC #206100	O	M	A Randomized, Double-Blind, Multicenter Study of Denosumab Compared with Zoledronic Acid (Zometa®) in the Treatment of Bone Metastases in Men with Hormone-Refractory Prostate Cancer (20050103)
Baker KC #206072	O	M	A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Phase 3 Study of Denosumab on Prolonging Bone Metastasis-Free Survival in Men with Hormone-Refractory Prostate Cancer
Baker KC #205006	O	M	A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Bone Fractures in Men with Prostate Cancer on Androgen Deprivation Therapy (Protocol #G300203)
Baker KC #204091	O	M	A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate AMG 162 in the Treatment of Bone Loss in Subjects Undergoing Androgen-Deprivation Therapy for Non-Metastatic Prostate Cancer
Baker KC #204025	C	M	An Evaluation of Semen Characteristics after 40 Weeks Daily Dosing with 20 mg Tadalafil
Baker KC #205119	O	L	Expression of CXCR4 in Archived Prostate Cancer Specimens and its Association with Patient Demographics, Pathologic Results, and Outcomes
Baker KC #205017	O	A	Madigan Army Medical Center Advanced Laparoscopic Training Using the Pig ( <i>Sus scrofa</i> )
Baker KC #204121	T	L	Prevalence of PCR Detectable Human Papillomavirus (HPV) in Sexually Active Males - A Comparison of Specimen Collection Methods and Genitourinary Sites
Baker KC #206039	O	M	SEER Rapid Response Surveillance Study #5, Prostate Cancer Therapy Selection (PCATS) Study
Baker KC #204120	O	L	The Effect of Flexible Cystoscopy on the Serum PSA Values
Baker KC #205040	O	L	The Epidemiology of Nephrolithiasis in Soldiers Returning From Operation Iraqi Freedom
Baker KC #204079	O	M	Uniformed Services University National Prostate Cancer Database for the Center for Prostate Disease Research (CPDR) with Patterns of Care, Outcomes, and Prognostic Analyses, Protocol Number GT90CM
DeCastro BJ #202065	O	M	Oral Ketoconazole For Prevention Of Postoperative Penile Erection, A Prospective, Randomized, Double Blind Trial
DeCastro BJ #205136	O	L	The Incidence of Infection and Stent Colonization in Patients With and Without Strings
Nelson DM #205076	O	L	Madigan Army Medical Center's Current Clinical Practice and Experience With Osteopenia And Fractures In Men Treated With Androgen Deprivation Therapy
O'Reilly KJ #203053	C	M	A Clinical Trial Evaluating the Safety and Efficacy of ABX-EGF in Patients with Hormone Resistant Prostate Cancer Elevated PSA With or Without Metastasis, Protocol Number ABX-0310

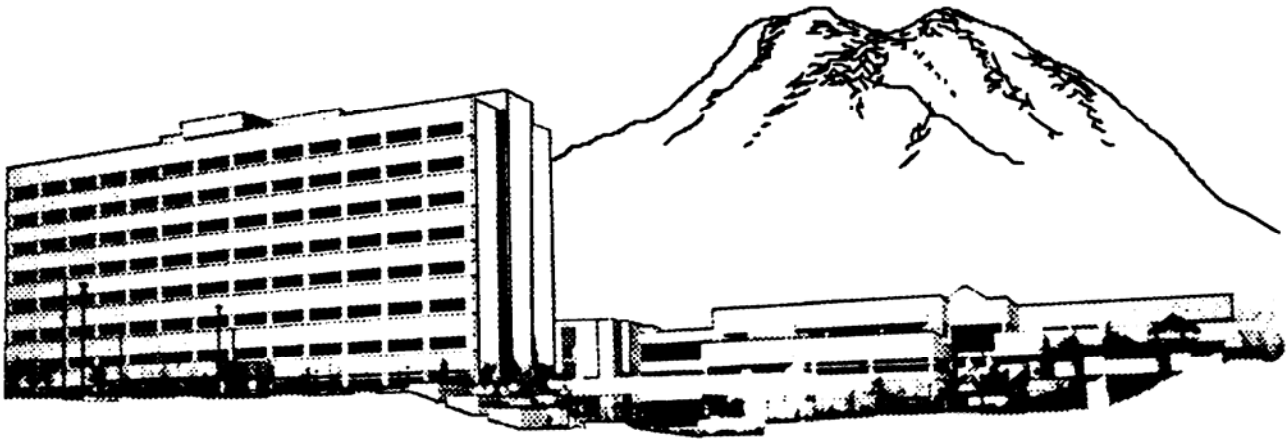
<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b><u>Title</u></b>
O'Reilly KJ #205033	C	M	A Phase 2, 8-Week, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study Evaluating the Efficacy, Tolerability and Safety of [S,S]-Reboxetine (PNU-165442G) for Stress Urinary Incontinence in Women, Protocol A6061023
O'Reilly KJ #206024	T	M	A Twelve-Week Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Forced Titration, Proof of Concept Study to Assess the Efficacy, Safety and Tolerability as well as the Pharmacokinetic Profile of 60 mg and 120 mg of GW679769 (GW679769) administered once daily vs. Placebo in Women with Overactive Bladder
O'Reilly KJ #204116	C	M	Phase 2, Multi-Center, Randomized, Double-blind, Placebo-Controlled, 3 Arm, 12-Month Study to Evaluate the Effects of GPI 1485 on Erectile Function in Patients Undergoing Bilateral Nerve-Sparing Radical Retropubic Prostatectomy for Prostatic Carcinoma, Protocol Number 0501-0202
Peterson AC #205073	O	M	A Phase 2, Randomized, Multicenter, Placebo-Controlled, Double-Blind Dose-Ranging Clinical Trial to Study the Efficacy and Safety of 5, 15, or 25 mg/day of CyPat™ (Cyproterone Acetate) for the Treatment of Hot Flashes following Surgical or Medical Castration of Prostate Cancer Patients, Protocol #DR-PCA-201
Peterson AC #205086	C	M	A Randomized, Double Blind, Placebo and Active-Controlled Efficacy and Safety Study of SSR240600C, in Patients with Overactive Bladder or Urge Urinary Incontinence, Protocol # ACT 5190
Peterson AC #205116	T	M	A Randomized, Double-Blind, Parallel-Design, Placebo Controlled Study to Evaluate the Effects of 5 mg Tadalafil (IC351, LY450190) and 50 mg Sildenafil Administered Once Daily for 6 Months on Visual Function in Healthy Subjects or Subjects with Mild Erectile Dysfunction, Protocol H6D-MC-LVGO
Peterson AC #205027	O	M	A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Prostate Cancer in Men with High Grade Prostatic Intraepithelial Neoplasia (PIN)
Peterson AC #203042	O	M	A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5 mg Administered Orally Once Daily for Four Years to Reduce the Risk of Biopsy-Detectable Prostate Cancer, Protocol Number ARI40006
Peterson AC #205135	O	L	Acute Urinary Retention and the Role of Fill and Pull Voiding Trials
Peterson AC #206031	O	L	Adult Circumcision: Template vs Standard Sleeve Technique
Peterson AC #206117	O	L	Comparison of Non-Contrast Abdominal Computed Tomography (CT) to Contrast CT, Intravenous Pyelography (IVP) and Nuclear Renal Scan for Determination of Renal Function: A Retrospective Review
Peterson AC #202122	O	L	Followup of Testicular Microlithiasis in an Asymptomatic Population
Peterson AC #204078	O	M	Long-Term Open-Label Extension Trial for Subjects Completing the Phase 3 Trial of Fesoterodine (SP584) for the Treatment of Overactive Bladder Syndrome

<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b><u>Title</u></b>
Peterson AC #206102	O	M	Phase II, multicentre, randomised, double-blind, placebo-controlled, pilot study to determine proof of efficacy, safety, tolerability and pharmacokinetics of intravesical PSD597 in the symptomatic management of interstitial cystitis/painful bladder syndrome (IC/PBS)
Peterson AC #204032	O	M	Prospective, Observational Registry and Patient Survey of the Management of Men with Symptomatic Benign Prostatic Hyperplasia (BPH): BPH Registry and Patient Survey Protocol #L8890
Peterson AC #204086	O	M	Prospective, Open-Label, Non-Comparative, Multi-Center Study to Evaluate the Efficacy and Safety of Ciprofloxacin Extended-Release (Cipro-XR) 1000 mg Tablets Given Once Daily for 7 to 14 Days in the Treatment of Patients 18 Years or Older with Complicated Urinary Tract Infections Caused by Pseudomonas Aeruginosa and Other Common Uropathogens
Peterson AC #203081	O	M	Study of the Safety and Effectiveness of the Mentor Two-Piece Inflatable Penile Prosthesis, Protocol Number U108-802-4
Pugliese JM #205088	O	L	The Value of Resistive Index: A Longitudinal Study of Confounding Variables and Their Impact - A Pilot Study

#### **VASCULAR SURGERY, DEPARTMENT OF SURGERY**

Andersen CA #206012	O	M	A Comparative Prospective, Randomized, Double-Masked, Parallel Group, Sham-Controlled Trial of MIST Therapy for the Reduction of Pain in Chronic Lower Extremity Ulcers
Andersen CA #203079	C	M	A Double-Blind, Randomized, Parallel Group, Placebo-Controlled Study to Evaluate the Safety and Efficacy of NM-702 in Subjects with Intermittent Claudication, Protocol Number NCI-IC-0201
Andersen CA #206094	O	M	A Multi-Center, Double-Blind, Randomized, Parallel, Vehicle-and Standard Care-Controlled, Dose-Ranging Study Assessing the Safety and Efficacy of MRE0094 Gel When Applied Topically for 90 Days to Subjects with Diabetic, Neuropathic, Foot Ulcers
Andersen CA #205111	T	M	A Phase 3, Randomized, Double-Blind, Multinational Trial of Intravenous Telavancin Versus Vancomycin for Treatment of Complicated Gram Positive Skin and Skin Structure Infections with a Focus on Patients with Infections Due to Methicillin-resistant Staphylococcus aureus 0018
Andersen CA #200088	C	L	A Prospective, Randomized Study Comparing the Outcome of Carotid Endarterectomy Using New Generation Dacron or Expanded Polytetrafluoroethylene (e-PTFE) Carotid Patching
Andersen CA #202086	O	M	A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Diabetic Foot Ulcers (Protocol VAC2001-08)
Andersen CA #202115	C	M	A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Amputation Wounds of the Diabetic Foot, Protocol No. VAC2001-07
Andersen CA #203055	O	M	A Randomized, Controlled, Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Pressure Ulcers, Protocol Number VAC2001-01
Andersen CA #205010	O	M	Linezolid In The Treatment Of Subjects With Complicated Skin And Soft Tissue Infections Proven To Be Due To Methicillin-Resistant Staphylococcus Aureus

<b><u>Prin. Invest.</u></b> <b><u>#Protocol No.</u></b>	<b><u>S</u></b>	<b><u>T</u></b>	<b>Title</b>
Andersen CA #206071	O	M	Phase 3, Multicenter, Multi-National, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Alfimeprase in Subjects with Acute Peripheral Artery Occlusion (NAPA-3)
Andersen CA #205091	O	L	The Prevalence and Progression of Carotid Artery Stenosis in Patients Undergoing Radiation for Head and Neck Cancer
Andersen CA #203017	C	L	The Prevalence of Three Major Stroke Risk Factors in an Enrolled Medicare Population
Roukis TS #206127	O	M	A phase 2B long-term, randomized, open-label, safety and tolerability trial comparing [S,S]-Reboxetine (PNU-165442G) with routine care in patients with chronic painful diabetic peripheral neuropathy (DPN) Study Number A6061031
Roukis TS #206111	O	M	Pivotal Study to Evaluate the Efficacy and Safety of Dermal - Living Skin Replacement (Dermal - LSR) in the Treatment of Chronic Diabetic Foot Ulcers
Starnes BW #206070	O	M	A Two-Part, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Study to Evaluate the Effect of Simvastatin, Losartan, and Pioglitazone on Cardiovascular Disease Biomarkers in Lower Extremity Atherosclerotic Plaque Excised from Patients with Peripheral Arterial Disease
<b>WEED ARMY COMMUNITY HOSPITAL</b>			
Wheeler GA #205049	C	M	A Phase 2 Study to Evaluate the Reactivity and Tolerability of Intradermally Administered Doses of Coccidioidin in Human Subjects in a Target Population



## Detail Summary Sheets

Department of Anesthesia & Operative  
Services



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206121	<b>Status:</b> Ongoing
<b>Title:</b> Comparison of Direct Versus Indirect Laryngeal Views using the Video Laryngoscope During Standard Intubation Procedures		
<b>Principal Investigator:</b> LTC Joseph P. Miller, MC		
<b>Department:</b> Anesthesia & Operative Services		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 8/30/2006 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives of this study are to determine whether or not the indirect laryngeal view offered by the video laryngoscope is superior to view seen by direct laryngoscopy, the video laryngoscope offers improved anatomical views to the student during intubation training and the video laryngoscope offers improved means of providing external laryngeal manipulations to facilitate intubation.

**Technical Approach:** All patients intubated with the video laryngoscope will be entered into this study. The data collection sheet will be completed at the conclusion of intubation by the practitioner. No additional testing, or any medical interventions or practice outside the normal operating procedure will be employed. The only difference in patient care with participants in this study versus the currently employed airway management with the video laryngoscope, will be that the intubator will complete a questionnaire at the conclusion of the intubation process. No identifiers of the patient or practitioner will be on the questionnaire.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee, effective 30 August 2006.

### Detail Summary Sheet

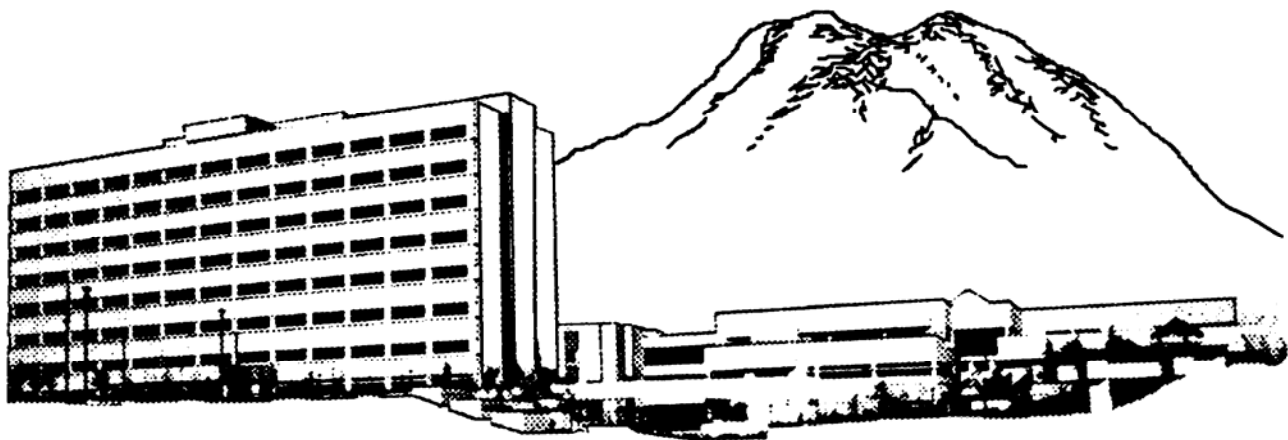
<b>Date:</b> 30 Sep 06		<b>Number:</b> 204010	<b>Status:</b> Completed
<b>Title:</b> Evaluation of the Combat Medic Skills Validation Test			
<b>Principal Investigator:</b> LTC Joseph P. Miller, MC			
<b>Department:</b> Anesthesia & Operative Services		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL (Ret) Eileen A. Hemman, PhD; COL David Gillingham, MC; COL H. Quigg Davis, USA			
<b>Start - Completion:</b> 1/13/2004 - Jul 2005		<b>Funding:</b> Triservice Nursing Research Program via The Geneva Foundation	<b>Periodic Review:</b> 10/14/2005

**Study Objective:** (1) Operationalize, standardize, and centralize the combat medics' validation testing as outlined in the TC (Training Circular) 8-800 using the collaboration of the joint medical training center and the simulation center. (2) Evaluate the psychometric properties of the SACMS-VT. (3) Test a random sample of battlefield medics (91W) to assess their combat medical readiness skills using the SACMS-VT.

**Technical Approach:** This study will employ a descriptive, prospective design using various instrument-testing techniques in which the reliability and validity of the SACMS-VT will be tested. Once the initial reliability and validity is established, a representative, random sample of units on Ft. Lewis with 100 91Ws that are scheduled for deployment within the next 1-2 years will be recruited to take the SACMS-VT. The specific aim of this study is to evaluate the psychometric properties of the SACMS-VT.

**Progress:** 49 subjects were enrolled in this study. Validity - Performance skills with a CVI < .75 were needle chest decompression, combitube® insertion, and AED (automatic external defibrillator). The skill of splinting was recommended for addition to the SACMS-VT. Reliability – There was high intra and inter-rater agreement on performance steps and skills with the exception of Bleeding/Shock Management, spinal immobilization (supine), and extraction. The average medics' score on the SACMS-VT was 68%. Subjects tested better on the medical skills than the trauma skills. When retested, there was significant improvement ( $t = 3.268$ ,  $df = 7$ ,  $p < .014$ , two tailed) in test results. **CONCLUSIONS/RECOMMENDATIONS:** The results support the validity and reliability of the SACMS-VT as an instrument to determine beginning level combat medic competency. The skills with lower validity were related to the raters' perception of medics' ability and may change when test score are improved. High reliability may be related to the expertise of the raters in this study and may change when raters of varying skill levels are used. It is highly recommended that the critical item passing criteria be used for training only and that the critical item designation be used for training only. For testing purposes, critical items should be if the medic increases a casualty's injuries during treatment or causes death through inaction or wrong action.

**IMPLICATIONS:** More research is needed to determine the combat medical readiness of 91Ws Army wide, as this subject population was characteristically novice medics with little experience.



## **Detail Summary Sheets**

Department of Clinical Investigation

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203122	<b>Status:</b> Expired
<b>Title:</b> Establishment of a Limb Regeneration Program Using Notophthalmus viridescens (newt) as the Model Organism and the Creation of a Transgenic N. viridescens Strain		
<b>Principal Investigator:</b> Jeff M. Bullock, M.S.		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jason A. Grassbaugh, MC		
<b>Start - Completion:</b> 9/10/2003 - Sep 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/13/2006

**Study Objective:** Establish a limb regeneration research program using *Notophthalmus viridescens* as a model organism. Create the first transgenic newt, expressing a LacZ or GFP marker protein.

**Technical Approach:** Limbs or blastemas are amputated with sharp iridectomy scissors (or suitable analog) and the epidermis is generally trimmed back to facilitate regeneration. Limb regeneration results in a fully formed (albeit small) limb within 4-6 weeks. At this point, animals will be returned to a recovery population tank until the regenerated limb is full size (another 1-2 months), at which time they are returned to the general population tanks. Newts are maintained in dechlorinated tap water at 20-26C (or a salted variant) and fed live *Tubifex* worms (or some variant) biweekly. Animals to be culled (after 3 amputations, aged or infirm) will be anesthetized and killed by decapitation. Remains of non-transgenic and transgenic animals will be discarded in accordance with hospital policy. Hormonal stimulation for the purpose of egg production will consist of 880-100 IU of human chorionic gonadotropin administered with a 21 gauge needle by IP injection every other day into the abdomen of an adult female until the female deposits eggs. All work will be done while the animal is anesthetized in a solution of 0.1% w/v Tricaine (3-aminobenzoic acid ethylester methanesulfonate salt; Sigma MS222), and the animals are allowed to recover in a solution of 0.1% W/V sulphamerazine for 24 hours before being returned to a recovery tank. Both of these solutions are made using dechlorinated tap water.

**Progress:** This protocol expired on 9-14-06 and I am in the process of analyzing several blastemas from upper arm and wrist amputation sites for the presence of N-cadherin by western blot analysis and immunohistochemistry of frozen sections. Upon completion of my analysis I will submit a report of my results. If the results look encouraging I plan to write a companion protocol to further investigate the role N-cadherin may play in tissue regeneration.

An additional goal of this protocol was to create a transgenic newt. I have had limited success in this. However it was recently reported that a group out of Germany has produced a transgenic newt and the progeny from this animal are now available for purchase; thus negating the need for additional work toward this goal.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206122	<b>Status:</b> Ongoing
<b>Title:</b> Profiling of Proteins Extracted from Tissue Taken from Regenerating and Intact Notophthalmus viridescens Limbs Using SELDI		
<b>Principal Investigator:</b> Jeff M. Bullock, M.S.		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC		
<b>Start - Completion:</b> 9/13/2006 - Sep 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Our primary objective is to produce a series of protein profiles from regenerating and non-regenerating limb tissue. Protein profiles for each sample will be compared. Differences in the profiles will be suggestive for which proteins may be involved in tissue regeneration. Candidate proteins will be targeted for further research.

**Technical Approach:** Experimental arms will consist of the following: 1) Amputation followed by enervation at various time points 5, 15, and 30 minutes and 1, 6, and 20-24 hours and 2, 3, 4, 5, and 6 days. 2) Enervation only. 3) Neural transection followed immediately by amputation, followed by blastectomy. Blastectomies will be performed when the blastemas reach the early to mid-late bud stage, but before the pallet stage. 4) Amputation followed by blastectomy. Blastectomies will be performed when the blastemas reach the early to mid-late bud stage, but before the pallet stage. 5) Normal non-regenerating tissue taken from amputated limbs at time of amputation. For all operations animals will be anesthetized by soaking in a cold (4-10 C0) neutralized solution (pH 7.2 - 7.4) of 0.1% w/v Ethyl 3-aminobenzoate, methanesulfonic acid salt (MS222). Forelimbs will be amputated at the mid humerus or mid radius; ulna region and protruding bones trimmed using iridectomy scissors or a suitable analog. Amputation of the first forelimb will be followed immediately by the amputation of the opposite forelimb. Amputated limbs to be saved will immediately be put into cryogenic tubes and snap frozen in liquid nitrogen. Amputees while still anesthetized will be given 100 µl of Buprenex by IP injection at a dose of (0.01-0.03 mg/kg) diluted to a concentration of 3 X 10<sup>-4</sup> mg/ml with a lactate ringer solution adjusted to a mOsmol/L of 225 +/- 5 using a 5/8 inch 26 gauge needle. Following the Buprenex injection animals are placed on an ice pack covered with a paper cloth for 15-30 minutes before allowing them to warm and placed back into an aquarium. Nerves 3, 4, and 5 of the brachial plexus are the main nervous supply in the newt forelimb. In animals to be enervated these nerves will be removed by excision. Using the tip of a 5/8 inch 26 gauge needle an incision will be made on the ventral side of the forelimb that runs along the entire length of the limbs' proximal distal axis. The epidermis and surrounding muscle are pulled aside to expose the nerves and the rounded bore of the needle is inserted beneath the nerve bundles and pulled along the length of the nerve to free it from any connective tissue. Once the nerve has been exposed and freed it is excised using iridectomy scissors or a suitable analog. Excised nerves to be saved are immediately put into cryogenic tubes and snap frozen in liquid nitrogen. In some cases nerves 3, 4, and 5 will not be removed, but will instead be transected at the brachial plexus. A small incision at the brachial plexus will be made with the tip of a 5/8 inch 26 gauge needle and the nerves severed with iridectomy scissors or a suitable analog. Animals whose nerves were removed or transected while still anesthetized will be given 100 µl of Buprenex by IP injection at a dose of (0.01-0.03 mg/kg) diluted to a concentration of 3 X 10<sup>-4</sup> mg/ml with a lactate ringer solution adjusted to a mOsmol/L of 225 +/- 5 using a 5/8 inch 26 gauge needle. Following the Buprenex injection animals are placed on an ice pack covered with a paper cloth for 15-30 minutes before allowing them to warm and placed back into an aquarium. If necessary, as determined by the staff veterinarian, a second and third dose of Buprenex will be give at 20-25 hours post-op, and at 46-48 hours post-op. If possible these injections will be given without anesthesia. In all cases (amputations, enervation, and nerve

transections) if Buprenex fails to provide adequate pain relief (as determined by the staff veterinarian) we plan to try other post-op analgesics. Possible choices include: Butorphanol at 0.2-0.4 mg/kg by IP injection, 2% Lidocaine or Bupivacaine administered topically 3-6 hours post-op then as necessary for 24-48 hours. All post-op analgesic care decisions/changes will be at the discretion of the staff veterinarian. Blastemas are removed by transecting the blastemas at the amputation plane using iridectomy scissors or a suitable analog. Once the blastemas have been removed they are immediately put into cryogenic tubes and snap frozen in liquid nitrogen. Following blastema removal animals are placed on an ice pack covered with a paper cloth for 15-30 minutes before allowing them to warm and placed back into an aquarium. No post-op analgesics will be given after removal of blastemas. Depending on the experimental arm an animal is placed in it may under go multiple surgical procedures. However, once an animal has been used in one experimental arm it will not be used in a different experimental arm or reused in the same experimental arm. Animals that have reached the end point of an experimental arm will be euthanized as described below. Animals to be euthanized will be placed in a 0.1 to 1.0 % w/v buffered solution (pH 7.2-7.6) of MS222 for 15-30 minutes until completely sedated. Dose and length of time of MS222 exposure will be at the discretion of the staff veterinarian. Following sedation animals will be decapitated using iridectomy scissors or a suitable analog. All tissues including euthanized animals will be place in the hospital trash for disposal. Tissue to be saved will be snap frozen immediately upon removal. Proteins will be extracted from frozen tissue by sonication and maceration in a buffered lysis solution containing protease inhibitors. Cellular debris will be removed by centrifugation and protein concentration determined by colorimetric spectroscopy. Protein profiles will be done using SELDI. Protein profiles from regenerating blastema and non-regenerating limb tissue along with nerve tissue from regenerating and non-regenerating limbs will be compared. Differences in the profiles will be suggestive for which proteins may be involved in tissue regeneration. Candidate proteins will be targeted for further research.

**Progress:** This protocol received initial approval during a convened meeting of the IACUC on 13 September 2006, work will begin in FY 07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205031	<b>Status:</b> Ongoing
<b>Title:</b> Proteomic Analysis of Longitudinally-Collected Maternal Plasma Samples: Establishing the 'Pregnancy Proteome'		
<b>Principal Investigator:</b> CPT Michael J. Hartenstine, MS		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Patrick M. McNutt, MS; CPT Jeremy P. Celver, MS; LTC Peter G. Napolitano, MC; COL Jerome B. Myers, MC; CPT Daniel G. Cuadrado, MC; MAJ Jennifer L. Gotkin, MC; Danielle L. Ippolito, PhD; CPT Garth S. Herbert, MC; Heidi M. Cederholm, B.S.; Aspen M. Bergmann, B.S.		
<b>Start - Completion:</b> 3/23/2005 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** To determine the baseline proteome for a normal pregnancy and assess the changes in protein among maternal plasma samples.

**Technical Approach:** Investigators propose to collect samples at the first OB/GYN physician visit ( NLT 12 weeks), during the second trimester analyte screen (~16-22weeks), early third trimester (26-28weeks), late third trimester (~36-38 weeks), upon admission for labor and at 6-10\* weeks post-partum, as well as cord blood collected at delivery. Plasma will be longitudinally collected from 300 pregnant women to conduct a pilot analysis of 10 representative patients with uncomplicated pregnancies at 3 time points. The preliminary results will be used for an initial publication and to pursue more substantive funding for a detailed analysis. The samples will be available for collaboration with other researchers under the auspices of the IRB, and under the direction of the research operations service component of DCI.

**Progress:** This protocol remains open to enrollment with 121 patients enrolled at MAMC. Significant improvement was achieved with patient enrollment during FY06. Crude samples of seven women have been profiled, which yielded the beginnings of a proteomic fingerprint of pregnancy. In addition to profiling samples from uncomplicated pregnancies, several miscarriage samples have been profiled and two specific proteins have been observed to be elevated in miscarriage samples. Collection of clinical data has begun on the patient population to better characterize the samples in the tissue bank.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205044	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective Study of Pseudocholinesterase Activity in Patients with Fibromyalgia, Chronic Pain, Pelvic Pain and Hernias		
<b>Principal Investigator:</b> CPT Patrick M. McNutt, MS		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; CPT Kathleen M. Goings, MC; CPT Jeremy P. Celver, MS; MAJ Brian T. McKinley, MC; CPT Kyle C. Harner, MC; CPT Christopher S. Murphy, MC		
<b>Start - Completion:</b> 3/17/2005 - Nov 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2/22/2006

**Study Objective:** To determine if there is a correlation between levels of serum cholinesterase and acute and chronic pain.

**Technical Approach:** Five separate groups will be analyzed for this protocol. Group 1, hernia surgery, patients identified with an inguinal hernia who are scheduled for surgery with the Department of General Surgery will be enrolled following detailed pre-operative history and physical examination and standard pre-operative laboratory evaluation. Those enrolled in the study will fill out a questionnaire at the time of this appointment and be consented by a member of the study staff or resident. During their routine pre-operative blood draw an additional 3cc purple top tube will be collected and sent to DCI. There the specimen will be centrifuged and the serum will be collected and snap frozen for analysis.

Immediately post-operatively, while in the recovery room, a second blood draw will be performed and the sample likewise sent to DCI for processing. A third and final 3cc specimen will be collected at the two week routine follow-up appointment at which time a second questionnaire will be completed. Group 2-4, Chronic pain, Fibromyalgia and Pelvic pain, patients will be identified at the Anesthesia pain, Rheumatology and Gynecology clinic for eligibility for entry in the study protocol. Those who meet criteria will complete the study questionnaire and undergo a single 3cc blood draw. The blood will be collected in a 3cc purple top tube and transported to DCI for processing. Samples will be labeled with a patient number and diagnosis. Group 5, Normal controls, twenty normal control patients will fill out the study questionnaire and have a single blood draw. The specimen will be collected in a 3cc purple top blood and processed in DCI.

Sample handling and determination of PCE activity: Samples will be collected, processed, aliquoted in 100uL fractions and stored at -70 in DCI. SchEs are extremely stable molecules so short periods (<12hrs) between collection and processing should not interfere with measurements of enzyme activity. 20.0uL of serum are added to 40.0uL of a 25% sucrose solution containing 10mM Tris-formate (pH 9.0). 3.0uL are then separated by vertical flat bed polyacrylamide gel electrophoresis on a 6.5% T: 5.0% C gel using a borate-sulfate discontinuous buffer system. Following electrophoresis, the gel is equilibrated in 96mL Tris-chloride (pH 6.6) in the presence of FAST Red TR or Fast BLUE RR as the diazonium salt for five minutes with gentle agitation. Add 4.0mL of 1.0% sodium alpha naphthyl acetate in acetone solution (the substrate) and allow the reaction to proceed for ten minutes at room temperature with constant agitation. Stop the reaction with 10% acetic acid. The resulting insoluble diazonium complex bands mark esterase activity. Quantify the esterase activity by quantitative densitometry. Densitometric results are presented as the integrated area under the curve of each peak expressed in pixels. The bench researcher will have access to patient numbers only and will be unaware of the diagnosis. Results will be tabulated in a password protected spreadsheet for statistical analysis after completion of specimen collection.



**Progress:** Investigators are currently analyzing data for correlation between pseudocholinesterase activity in pain patients compared to normal patients. In addition we are optimizing the pseudocholinesterase activity assay and exploring other assays for determining whether changes in activity are associated with changes in protein levels of pseudocholinesterase or activation state. The protocol remains ongoing.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203092	<b>Status:</b> Expired
<b>Title:</b> Animal Tissue Use in Biomedical Research and Training		
<b>Principal Investigator:</b> MAJ Nancy L Merrill, VC		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 7/13/2003 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7/12/2006

**Study Objective:** To reduce live animal use in biomedical research or training at MAMC by facilitating animal tissue use as alternative research/training models, wher feasible. Objectives for individual projects proposed under this protocol will be defined in project addendum.

**Technical Approach:** In the past, personnel requesting authorization to conduct biomedical research or training using postmortem animal tissues have been required by the MAMC IACUC to submit a "stand alone" animal care and use protocol that describes the proposed tissue use, background, justification, animal care provisions, literature searched conducted all in accordance with federal animal welfare regulations. Many of the provisions and assurances contained in the DoD-mandated animal use protocol format did not apply to research or training activities using animal tissues only. The task of preparing full protocols and related animal use reports for such activities places an unnecessary burden on individuals wishing to reduce live animal use by justifiable utilization of animal tissues. The "alternative" use of postmortem animal tissues rather than live animals (Reduction or Replacement) can be significantly facilitated by streamlining the preparation, submission, tracking and reporting of such research or training activities under an umbrella or stand protocol that spells out universal conditions for animal tissue use. and identifies a Principal Investigator (PI) who is responsible for overseeeing these activities.

**Progress:** Two amendments were submitted during FY 2006 to collect tissue samples. Muscle tissue samples were collected from animals undergoing IACUC approved terminal procedures. Muscle tissue was used to test new tissue preservation media. Blood samples were collected as non-terminal procedures from animals kept at DCI for training purposes. The blood samples were used for combat casualty training in transfusion procedures in protocol 204058. Protocol expired as of 12 Jul 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206109	<b>Status:</b> Ongoing
<b>Title:</b> Animal Tissue Use in Biomedical Research and Training		
<b>Principal Investigator:</b> MAJ Nancy L Merrill, VC		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Joren B. Keylock, MC; James R. Wright, BA, MT (ASCP); Donna J. Frey; CPT Matthew J. Eckert, MC		
<b>Start - Completion:</b> 7/12/2006 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To reduce live animal use in biomedical research or training at MAMC by facilitating animal tissue use as alternative research/training models, where feasible. Objectives for individual projects proposed under this protocol will be defined in project addendum.

**Technical Approach:** In the past, personnel requesting authorization to conduct biomedical research or training using postmortem animal tissues have been required by the MAMC IACUC to submit a "stand alone" animal care and use protocol that describes the proposed tissue use, background, justification, animal care provisions, literature searched conducted all in accordance with federal animal welfare regulations. Many of the provisions and assurances contained in the DoD-mandated animal use protocol format did not apply to research or training activities using animal tissues only. The task of preparing full protocols and related animal use reports for such activities places an unnecessary burden on individuals wishing to reduce live animal use by justifiable utilization of animal tissues. The "alternative" use of postmortem animal tissues rather than live animals (Reduction or Replacement) can be significantly facilitated by streamlining the preparation, submission, tracking and reporting of such research or training activities under an umbrella or stand protocol that spells out universal conditions for animal tissue use and identifies a Principal Investigator (PI) who is responsible for overseeing these activities.

**Progress:** Two amendments were submitted for tissue collection from other IACUC approved terminal training protocols. One was for muscle tissue to test transport medium under different conditions and the other was for arteries, veins, hearts, and eyes to be used to train surgical and ophthalmological residents in various techniques specific to their specialties.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203076	<b>Status:</b> Terminated
<b>Title:</b> Breeding Colony of Red-Spotted Newt ( <i>Notophthalmus viridescens</i> )		
<b>Principal Investigator:</b> MAJ Nancy L Merrill, VC		
<b>Department:</b> Clinical Investigation		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Patrick M. McNutt, MS; Steven O. Gibson; SPC Timothy S. Montminy		
<b>Start - Completion:</b> 5/21/2003 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/11/2005

**Study Objective:** To provide newts of the appropriate type and age to meet the needs of IACUC approved protocols.

**Technical Approach:** Newts will be purchased for the breeding colony and raised in an aquarium or polycarbonate cages with lids to prevent escape. Newts will be provided an environment that is mostly water but will have areas to leave the water, hide and interact with each other. Breeding can be controlled based on the number of animals in each container and the temperature of the water. Newts normally breed in the fall and winter when the water is colder. Thus by regulating the water temperature up or down by a few degrees, mating behavior can be altered to regulate offspring production. Eggs will be removed from the adult containers to prevent them from being eaten. Eggs may then be used for some studies while others will be allowed to continue to develop into adults for use as breeders or for other IACUC approved protocols. The larva are terrestrial and will be housed in polycarbonate cages with plant material.

The tracking and accounting of each animal will be part of the daily colony management. Each animal entering the colony, whether purchased or propagated, will be assigned an identification number. The animal will be tracked as it is introduced into the breeding colony, transferred to an experimental protocol, culled as excess to experimental requirements, or lost perinatally. Only the breeding stock and animals culled as excess or lost perinatally will count against the breeding protocol. All animals transferred to an experimental or training protocol will be counted against that protocol. At 4 to 5 years of age, breeders will be euthanized and replaced with new breeding stock. New breeding stock will be raised for replacement of breeding stock along the way. Newts can have a long lifespan but it is not uncommon to have many lost younger due to escaping into an area where they become dessicated and the fact that newts are very susceptible to any toxic substances.

**Progress:** *Notophthalmus viridescens* did produce viable eggs for protocol #203122.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206091	<b>Status:</b> Ongoing
<b>Title:</b> MAMC Rodent and Rabbit Quality Assurance and Sentinel Program		
<b>Principal Investigator:</b> MAJ Nancy L Merrill, VC		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MSG Karen L Van Loon; SGT Anita J S Teadt; SPC Miemie T Phillips; SPC Shayla M Phyll; Shelley L Spahn-Bridges; Jennifer L. Theis		
<b>Start - Completion:</b> 5/10/2006 - May 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The purpose of this protocol is to provide a reliable program for preventing the introduction of adventitious organisms into the MAMC rodent and rabbit colonies. This will be accomplished by sampling species from selected sources as they are received into the facility. Suspect groups of animals will be quarantined based on vendor health reports, and their release from quarantine will depend on results of quality assurance tests. Continuous health monitoring or surveillance will be accomplished by housing sentinel animals in the animal rooms, and then periodically submitting them for quality assurance testing.

**Technical Approach:** Experiment 1: Sentinel Surveillance: Sentinel animals must be of known health status as indicated below in para. V.3.3.7. For this purpose, sentinel mice will be purchased from JAX or Harlan and sentinel rats from JAX or Harlan. Sentinels will be kept in the colony at least one month before they are sacrificed and tested, allowing for any potential exposures and subsequent seroconversion to occur. Complete procedural techniques are outlined in LARS Quality Assurance of Rabbits and Rodents and Sentinel Surveillance SOPs.

a. Mice: A minimum of 16 mice, 4 cages of 4 mice per cage, will be placed in each occupied mouse room initially (preferably at the beginning of the calendar year). During cage changing soiled bedding will be collected from at least 2-3 cages off of each rack in the room and placed in a clean container and well mixed. The sentinel animals will be changed last. A handful of the mixed dirty bedding will be broadcast over the clean bedding of a fresh cage before adding the sentinel animals to the cage. Sentinel cages will be unfiltered, as open to the room as possible. One cage of mice will be sacrificed each quarter. At the mid-point of the quarter, 2 of 4 mice in the cage will be sacrificed for serology screening. The blood will be pooled from those 2 animals and sent to Research Animal Diagnostic Laboratory (RADIL), University of Missouri. At the end of the quarter, the remaining 2 mice will be sacrificed for comprehensive testing to include serology and pathology by RADIL and in-house parasitology (including examination of pelts for external parasites). Feces from each room will be pooled every six weeks and submitted for *Helicobacter* testing by RADIL.

1) Should any rooms be used for breeding, sentinel mice will be selected from the indigenous population. Retired breeders will be used for serology, whereas parasitology and pathology will be performed on weanlings and young adults.

2) Extra animals (2 per 16 animals) will be ordered with each sentinel purchase, if not from JAX or Harlan. See section V.1.2 These animals will be sacrificed within one day of delivery and submitted for Quality Assurance Procedures described in para. V.4.4.2.

b. Rats: Sentinel rats will be managed in a similar manner, except they may be housed singly. For long-term housing of rats (greater than two months), two sentinel rats will be added to each occupied rat room initially. The cages will contain a sample of soiled bedding from each rack of animals in the room each time the cages are changed, similar to the procedures for changing mice. At the mid-point of the quarter 1 rat will be sacrificed for serology and parasitology, and 1 rat will be sacrificed for a comprehensive pathologic examination, serology and parasitology at the end of the quarter. Feces from each room will be pooled every six weeks for floatation and testing for *Helicobacter*. One additional rat will be ordered with each sentinel rat

purchase. This animal will be sacrificed within one day of delivery and submitted for Quality Assurance Procedures described in V.4.4.2.

c. In the face of a potential infectious disease outbreak, these sampling timetables are compressed under the direction of the Chief, Laboratory Animal Resources Service, and are based on pathogenesis of the suspected agents.

**Experiment 2: Quality Assurance Sampling:** For the approved vendors (Harlan and Jackson Labs), the Chief, LARS will review and sign diagnostic health reports for the incoming shipment to ensure that the incoming animals are free of adventitious organisms. These reports must be current within six months. For other vendors, quality assurance will be performed on animals from the same barrier and/or species/strain as those ordered.

In the event that animals from any approved vendors are found to be the source of an adventitious organism within the animal colony, two extra mice/rats will be ordered with each shipment and processed for QA testing until it is determined that additional testing is no longer necessary. This determination will be based upon a current literature review of the epidemiology and pathophysiology of the individual organism(s) in question.

If rodents or rabbits are received from an unknown vendor, they must have a diagnostic health report current within six months. For these unknown vendors, additional animals (a minimum of 3-5%, but not less than two animals, at the discretion of the Chief, LARS, of the same strain, facility, and barrier/location will be ordered with each shipment and will be submitted for quality assurance testing. The Chief, LARS will base his/her decision upon a current literature review of the epidemiology and pathophysiology of the individual organism(s) in question and upon current quality assurance standards within the industry.

**Data Analysis:** Statistical analysis will not be necessary in this protocol. Results of serology, parasitology, and pathologic examination will be used to determine whether or not adventitious organisms enter the animal colony, their spread, and whether control measures are effective in preventing and eliminating these agents.

**Progress:** Four C57BL were placed as sentinels in the mouse holding room. Two were submitted for analysis and found negative for pathogens. Eight DBA/2 were placed in the nude mouse room. Two were submitted for analysis and came back positive for a newly identified virus, Murine Norovirus (MNV). This finding was discussed with the supplier and their colony has been found to be positive for this non-pathogenic virus in immunocompetent mice. Transmission to the nude mice is unlikely given methods of husbandry. A new source for sentinels will be identified for future use.

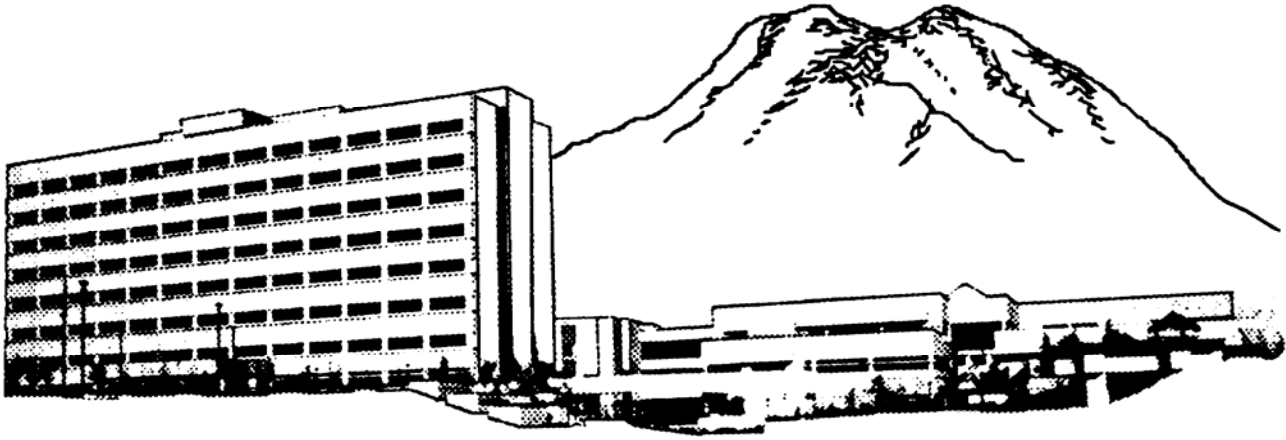
## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203075	<b>Status:</b> Terminated
<b>Title:</b> Mouse (Mus Musculus) Breeding Protocol		
<b>Principal Investigator:</b> MAJ Nancy L Merrill, VC		
<b>Department:</b> Clinical Investigation	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Patrick M. McNutt, MS; Steven O. Gibson; SPC Timothy S. Montminy		
<b>Start - Completion:</b> 5/21/2003 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/11/2005

**Study Objective:** To establish a breeding colony of mice for future use in research protocols.

**Technical Approach:** LacZ<sup>+</sup> and normal mice will be purchased from Jackson Labs (a commercial vendor with an established health monitoring history) to establish the breeding colonies. The colony will start with up to 6 females and 3 males of each strain. The female mice will be housed in groups when they are not pregnant or nursing pups. After they are used as breeders for the first time, the male mice will be group housed except when paired with females for mating. Propagation will be carefully managed: breeders will be paired only when there is a need for offspring for an experimental protocol. Excess offspring not needed for the experimental protocol for which they were bred will be transferred to other experimental or training protocols when possible, used as sentinels or replacement breeders. If mice are not needed for any other protocols, the excess offspring will be euthanized and tissues from these excess offspring will be made available to other investigators for use on approved research. When mice are required for use on an approved protocol, male and female(s) of the desired strain or stock will be housed together for approximately one week and then separated. The female mouse will be provided with nesting material in addition to the normal bedding used. The offspring will remain in the cage with the female until they are used in an experimental protocol, culled, or weaned at approximately 21 days of age. After the pups are removed, the female will be returned to pair housing as soon as possible. Records will be maintained to show the breeding history of each animal, i.e., which animals were paired, dates pairs were put together and separated, date of birth, number of pups produced, number lost perinatally, number euthanized, etc. The tracking and accounting of each animal will be part of the daily colony management. Each animal entering the colony, whether purchased or propagated, will be assigned an ID number. Only the breeding stock and animals culled as excess or lost perinatally will count against the breeding protocol. All animals transferred to an experimental or training protocol will be counted against that protocol. At 12 to 18 months of age, breeders will be euthanized and replaced with new breeding stock. Additionally, if we identify female breeders that are unable to effectively rear their pups, these animals may be euthanized prior to the stated ages. Breeders can be either homozygous or heterozygous: thus, progeny need to be tested by a simple enzyme assay (performed on tail/ear punches in our laboratory) for the presence of the LacZ enzyme. Negative homozygotes can be incorporated in the concurrent wild-type colony. The total number of experimental animals initially requested on the protocol is 250/yr for three years (200 research subjects and 50 breeding animals/strain). The mothering ability of the females of both strains is excellent and Jackson Labs reports neonatal mortality to be less than 5%. If the percentage of pups that die or are euthanized exceeds 20% this will be reported to the IACUC. If different stocks or strains are required for protocols subsequently approved by the IACUC, additional animals will be requested by an amendment to this protocol or by separate protocol.

**Progress:** Breeding colony started with 29 mice and 14 wild type were purchased to maintain colony. A total of 315 wild type mice and 35 Rosa mice were weaned and transferred to protocol 205080.



## Detail Summary Sheets

### Hospital Dental Clinic



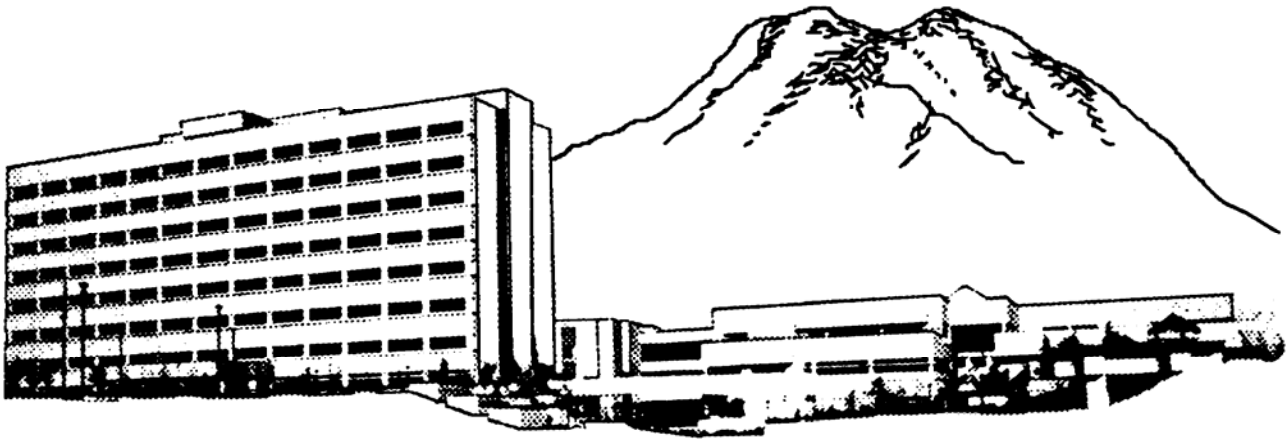
## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203116	<b>Status:</b> Ongoing
<b>Title:</b> Host Response Gene 203014 in Military Populations		
<b>Principal Investigator:</b> MAJ Scott W. Burgan, DC		
<b>Department:</b> Dentistry	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Paul O. Francis, DC; Richard P. Darveau, Ph.D.; MAJ Douglas R. Dixon, D.M.D., M.S.D; COL (Ret) Robert B. O'Neal, DMD, MEd, MS; LTC Edward B. Fowler, DC; Frank A. Roberts, D.D.S., Ph.D.; Beverly Dale, Ph.D.		
<b>Start - Completion:</b> 9/12/2003 - Sep 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** To determine the incidence of polymorphisms (mutations) in bacterial receptors between periodontitis-affected and periodontally healthy dental patients.

**Technical Approach:** This study will look at a single nucleotide polymorphisms (SNP's) found in hTLR and other host response genes that will be examined for their association with periodontitis in the Hispanic and African American military population. Approximately 450 patients will be enrolled in this study here at MAMC 225 periodontically healthy and 225 periodontitis-affected that are 18 years of age and older. The frequency of different TLR pleomorphisms found in the populations will be determined for their association to periodontitis using genomic DNA isolated from cheek swab samples and compared for binomial proportions in periodontally healthy and diseased subjects. This information will aid the army in identifying those individuals at risk for developing periodontitis and will contribute to better health care by providing new information concerning the molecular basis of increased susceptibility to and severity of periodontal disease.

**Progress:** This protocol remains ongoing with only 30 samples gathered during FY06. The continuing challenge is in having personnel for sample gathering. With the high OPS Tempo at Fort Lewis priorities have often been in other areas. There has also been a loss of some personnel from the UW side of the house. The nature of this study is such that there is no problem with an extended period of sample gathering. It is taking longer than anticipated but is still a viable and important study to continue.



## **Detail Summary Sheets**

Department of Emergency Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204087	<b>Status:</b> Terminated
<b>Title:</b> A Prospective Study on the Effects of Ginkgo Biloba on Bleeding Times		
<b>Principal Investigator:</b> MAJ Jimmy L. Cooper, MC		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Wesley G. Zeger, MC; Benjamin B. Betteridge, MD		
<b>Start - Completion:</b> 9/14/2004 - Jul 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/28/2005

**Study Objective:** To determine if ginkgo biloba significantly affects the bleeding times in young healthy volunteers.

**Technical Approach:** Twelve healthy volunteers will be enrolled in this prospective study. Each subject will serve as their own control. Baseline bleeding times will be drawn using the Simplate test procedure. Each subject will take ginkgo biloba for one week and then have a repeat bleeding time done. This data will then be analyzed using the pair t-test to determine if ginkgo biloba significantly affects bleeding times.

**Progress:** The protocol was eventually terminated by the Chief, Department of Emergency Medicine in June 2006, as the Simplate test procedure was discontinued at MAMC and it was no longer feasible to conduct the study. Four subjects were enrolled during FY05.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206063	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Study of Capnography in Emergency Department Procedural Sedation		
<b>Principal Investigator:</b> MAJ Mark A. Denny, MC		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Joseph P. Mazzoncini, MC; LTC David A. Della-Giustina, MC		
<b>Start - Completion:</b> 6/7/2006 - Apr 2007	<b>Funding:</b> Oridion via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if capnographic data recognizes respiratory depression during emergency department sedations that are not clinically recognized and whether these events are clinically important.

**Technical Approach:** This study is a prospective, blinded, randomized trial evaluating emergency physicians' use of capnography during consecutive procedural sedations on patients who sign informed consent to participate. Approximately 22 emergency physicians would be asked to consent for this trial. The physician may or may not have access to the capnographic data with each sedation. The physician will then complete the sedation as typical. The emergency physician should continuously evaluate the patient during the sedation as they normally would, however, if not blinded to the capnographic data, they may use this to assist in their decision making processes. The nurse observing the sedation will record the time to recovery and have the patient fill out the visual analog scales evaluating injection pain recall, procedural recall, and patient satisfaction. The physician completing the sedation will record, level of sedation, number of clinically recognized respiratory depression events, recognized complications, clinician interventions, and physician satisfaction. Study investigator will analyze the stored capnographic data looking for unrecognized complications and respiratory depression events. The groups will be compared by complication rates, incidence of interventions, incidence of respiratory depression events, level of sedation, time to recovery, injection pain, procedural recall, physician satisfaction, and patient satisfaction. A p-value of less than 0.05 will be considered statistically significant. Data will be analyzed using chi square, ANOVA, Kruskal-Wallis, and Mann-Whitney U-test methods.

**Progress:** This protocol is open to enrollment, with no patients enrolled during FY06. The data recording device is not functioning properly and has been sent back to the manufacturer. Enrollment will be initiated when the data recording device is working.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206050	<b>Status:</b> Terminated
<b>Title:</b> Magnesium Sulfate for the Prevention of Etomidate Induced Myoclonus in Emergency Department Procedural Sedation		
<b>Principal Investigator:</b> MAJ Mark A. Denny, MC		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Joseph P. Mazzoncini, MC; LTC Benjamin P. Harrison, MC; CPT Joshua A. Carr, MC		
<b>Start - Completion:</b> Never approved	<b>Funding:</b> Oridion via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if pretreatment with magnesium sulfate is effective in preventing etomidate induced myoclonus during emergency department procedural sedation. To determine if capnographic data recognizes complications during emergency department sedations that are not clinically recognized and whether these events are clinically important.

**Technical Approach:** This study is a prospective, double-blind, placebo-controlled trial evaluating the usefulness of pretreatment with magnesium sulfate to reduce myoclonus induced by etomidate sedation in emergency department patients 18 years of age or older who need procedural sedation. Patients will be randomized to two groups of 58 patients each. The clinicians will be randomized to be blinded or not to capnographic data. Patients will receive either placebo or magnesium sulfate ninety seconds prior to sedation with etomidate. The nurse observing the sedation will record the time to recovery and have the patient fill out the visual analog scales evaluating injection pain recall, procedural recall, and patient satisfaction. The physician completing the sedation will record myoclonus incidence, level of myoclonus, level of sedation, recognized complications, unrecognized complications, clinician interventions, and physician satisfaction. The groups will be compared by percentage of myoclonus, level of myoclonus (mild, moderate, severe), level of sedation, time to recovery, complication rates, intervention rates, etomidate injection pain, procedural recall, physician satisfaction, and patient satisfaction. A p-value of less than 0.05 will be considered statistically significant. Data will be analyzed using chi square, ANOVA, Kruskal-Wallis, and Mann-Whitney U-test methods.

**Progress:** Soon after initial IRB approval with stipulations January 2006, the PI terminated this study due to issues with administration of Magnesium IV push when it was determined not to be feasible clinically.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206028	<b>Status:</b> Completed
<b>Title:</b> Application of the Wells Criteria to determine Pretest Probability of Pulmonary Embolism: A Retrospective Review of the practices of the Madigan Army Medical Center Department of Emergency Medicine		
<b>Principal Investigator:</b> CPT Gregory M. Johnston, MC		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Phu Tan Nguyen, MC; LTC Benjamin P. Harrison, MC		
<b>Start - Completion:</b> 12/14/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if MAMC emergency residents/staff are making use of explicit criteria, i.e. Wells criteria, versus utilizing an empirical method, i.e. drawing upon past experience, when determining the pretest probability of pulmonary embolism and to enhance awareness of the clinical utility of the Wells criteria, and thereby optimize the care of patients by preventing the use of inappropriate diagnostic tests.

**Technical Approach:** Emergency Department charts will be inspected for the presence of a history of the present illness (to account for immobilization, or hemoptysis), vital signs (to account for heart rate), past medical history (to account for malignancy, previous deep venous thrombosis or pulmonary embolism, or recent surgical intervention), and physical exam (to account for the presence of suspected deep venous thrombosis)-all noted components of the Wells criteria. It is imperative to note that charts lacking any of these findings will be considered empirically assessed.

**Progress:** This protocol was reported completed in June 2006. To date, 300 charts met all inclusion criteria for the study; 24 cases of deviation from appropriate risk stratification were identified: 8% empiric risk stratification:

- 5 with positive d-dimer and no follow-up study (none of patients signed out AMA)
- 9 with low pre-test probability that went straight to CTPA; 1 with positive CTPA for PE: 37.5%
- 8 with moderate pretest probability that underwent d-dimer testing prior to CTPA: 33%
- 2 with moderate pretest probability with d-dimer testing (all negative) and no additional testing

Of the 300 charts reviewed, a total of 24 documented cases of pulmonary embolism were noted. Of the 24 cases, 4 were inappropriately risk stratified-with 2 of the 4 cases experiencing a delay in disposition secondary to inappropriate risk stratification. The PI noted that this is preliminary data that is subject to additional analysis before conclusions can be drawn. It can be confidently posited, however, that the data indicates that additional resident education would prove to be beneficial.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206059	<b>Status:</b> Ongoing
<b>Title:</b> Causes and consequences of patients who left a busy Army Medical Center Emergency Department prior to evaluation by a qualified health care provider		
<b>Principal Investigator:</b> CPT Adam S. Nielson, MC		
<b>Department:</b> Emergency Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Christopher S. Kang, MD		
<b>Start - Completion:</b> 1/31/2006 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The purpose of this study is to, first, describe the characteristics of the large number of patients who register for care at the MAMC-ED, then subsequently leave prior to evaluation by a qualified provider. Describing the characteristics of these patients should help identify where the MAMC health care system can make quality improvement changes to improve patient health care and access to a qualified provider. Secondly, the nature of the acuity of the illnesses or injuries that this population of patients represents will be described to determine if patients with severe illness are being permitted to leave prior to evaluation, subjecting the hospital and its providers to unnecessary liability. Patients will be contacted to determine the outcomes of their illnesses; i.e., did the patients seek care elsewhere, return to the MAMC-ED, hospitalized, or did the illness/injury improve on its own.

**Technical Approach:** Patients who leave the Madigan Army Medical Center-Department of Emergency Medicine, prior to being evaluated will be contacted by phone by the investigators and asked a standardized series of questions regarding the nature of their illness, what they have done to address it, why they left the emergency department prior to formal evaluation, and what could have been done to prevent their leaving.

**Progress:** Nearly 200 patients participated in this protocol; although less than the original goal, the current number is larger than past studies both referenced and/or reviewed. Data analysis will be initiated to see if statistical significance has been achieved or whether or not the study should resume. A more accurate assessment should be available by the end of the year.

### Detail Summary Sheet

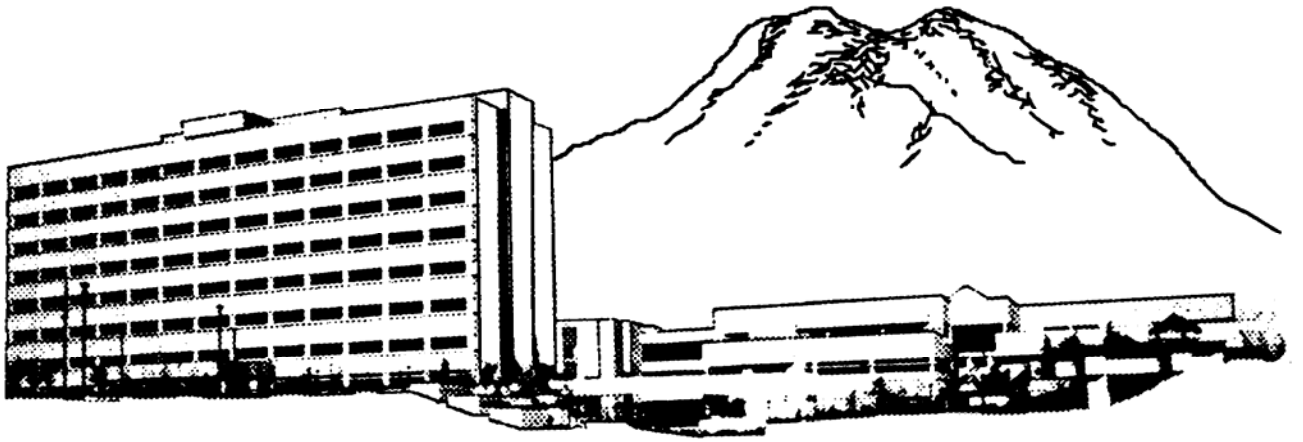
<b>Date:</b> 30 Sep 06	<b>Number:</b> 206078	<b>Status:</b> Ongoing
<b>Title:</b> Emergency Medicine/Combat Trauma Management Training Using Animal Models (Domestic Goat/ Capra hircus, Pig/Sus scrofa)		
<b>Principal Investigator:</b> MAJ Bradley N. Younggren, MC		
<b>Department:</b> Emergency Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Benjamin P. Harrison, MC; MAJ Brandon K. Wills, MC; Christopher S. Kang, MD; MAJ Robert B. Blankenship, MC; MAJ Melissa L. Givens, MC; CPT Jacob A. Roberts, MC; CPT Todd F. Baker, MC		
<b>Start - Completion:</b> 4/12/2006 - Mar 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To effectively train providers combat-relevant resuscitative skills, focusing on preservation of life, limb, critical organ function, and casualty stabilization.

**Technical Approach:** Training will utilize both inanimate (e.g. mannequin, cadaver, Sim Man, etc.) and live, anesthetized animal models. Whenever feasible, inanimate models will be used in place of live animals. Animal species used for this protocol will include goat and pig.

**Progress:** Three training labs were held in FY 2006, using 18 animal models and training 84 emergency medicine residents in emergency medicine and combat casualty procedures. Training is further enhanced by the use of simulation models at the Anderson Simulation Center. During the course of a three year residency, 1st year residents progress from trainees to instructors by their 3rd year. Residents graduate with tangible improvement of skills necessary to perform emergency medicine and combat casualty procedures.





**Detail Summary Sheets**

Department of Family Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205133	<b>Status:</b> Ongoing
<b>Title:</b> Prevalence of Hypertension in Active Duty Service Members		
<b>Principal Investigator:</b> COL Gary W. Clark, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LCDR Brian A. Smoley, MC, USN		
<b>Start - Completion:</b> 9/7/2005 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/14/2006

**Study Objective:** To use screening blood pressure measurements collected during mandatory wellness screenings to estimate the prevalence of hypertension in a population of active duty service members at Fort Lewis.

**Technical Approach:** This will be a retrospective, cross-sectional analysis of data collected on approximately 10,000 active duty service members who presented for wellness screenings through the I Corps Readiness and Outcomes Wellness Service (ICROWS) between January 1 and December 31, 2004. Data on measured blood pressure and self-reported age, rank, gender, race/ethnicity, and use of blood pressure medications will be collected from the ICROWS database without any inclusion of or reference to individual identifying information. Measured blood pressure and self-reported use of blood pressure medications will be used to estimate the prevalence of hypertension in the study population. Age-specific and age-adjusted prevalence of hypertension will be reported using descriptive statistics. Relationships between hypertension and demographic variables will be explored through bivariate and/or multivariate analyses.

**Progress:** Data on 15,391 study subjects has been analysed to estimate the prevalence of hypertension in the study population. A draft of the analysis is currently undergoing AMEDD public affairs review prior to being submitted for credit toward completion of a MPH degree at the University of Washington. The researchers anticipate keeping the protocol open for an additional year in order to allow for potential protocol modifications involving the collection of additional data to facilitate secondary analyses. Presentation of the results and/or submission for publication in a peer-reviewed journal are anticipated within the year.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205124	<b>Status:</b> Ongoing
<b>Title:</b> Racial Differences in Health Outcomes for Adults with Diabetes in a Military Setting		
<b>Principal Investigator:</b> LTC Telita Crosland, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 8/23/2005 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/10/2006

**Study Objective:** To evaluate health outcomes for diabetic patients based on race in a military setting.

**Technical Approach:** This study is a quantitative cross-sectional analysis of approximately 5000 adult patients in the MAMC diabetic database. Data to be recorded includes: race, age, rank, low density lipoproteins, hemoglobin A1C, blood pressure, micro albumin, and number of clinic visits. Descriptive statistical analysis will be used to determine if there is a statistical and clinical difference in health outcomes in the diabetic patient based on age.

**Progress:** This protocol has completed data collection and analysis, but remains ongoing to complete final manuscript.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204117	<b>Status:</b> Ongoing
<b>Title:</b> Impact of the Sole Prescriber Program on use of Opioid Medications and Quality of Life		
<b>Principal Investigator:</b> COL Diane M. Flynn, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Guy P. Runkle, MC; Steven J. Konicek, MD; Nancy A. Poffenberger, PAC, Ph; Claudia N. Swenson, PhD; Gary J. Revello, RPh; Helen E. Holt, ARNP; LTC Mary T. Bennett, AN; MAJ Elizabeth C. Shanley, MC		
<b>Start - Completion:</b> 8/31/2004 - Dec 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/14/2006

**Study Objective:** This protocol is designed to determine if enrollment of Madigan patients identified as being high utilizers of narcotic medication into a sole prescriber program results in a decrease in escalation of narcotic use and an improvement in patient satisfaction. Secondary objectives include determination of the impact of the sole prescriber program on continuity of care, utilization of services and quality of life.

**Technical Approach:** An estimated 50 MAMC patients who have received more than 7 prescriptions from the MAMC pharmacy for opioid medications per quarter during all of the first three quarters of FY2004 will be randomized into two groups: (1) immediate and (2) delayed enrollment in the Sole Prescriber Program. Patients randomized for immediate enrollment will be enrolled starting 1 October 2004. Delayed enrollment will begin 1 February 2005. The groups will be compared with regard to monthly dosage of opioid medications expressed in morphine equivalent dosage, number of prescribers of narcotics per patient, and several measures of utilization of clinical services. In addition, patient satisfaction and quality of life will be measured at baseline and after three months in both groups.

The following dependent variables will be compared between study groups using the paired t-test: (1) Change in morphine equivalent dosage of narcotics, (2) Mean number of prescriptions for narcotics per patient per quarter, (3) Mean number of prescribers of narcotics per patient per quarter, (4) Mean number of ER visits per patient per quarter, (5) Mean total MAMC visits per patient per quarter, (6) Mean total visits to health care facilities in community billed to TRICARE per patient per quarter, and (7) Score on quality of life survey. The following binary dependent variables will be compared between study groups using the McNemar's test: (1) At least one visit to primary care provider per quarter (Yes/No), and (2) Is a narcotic agreement recorded in the electronic medical record (Yes/No). The 5-item patient satisfaction survey will be analyzed using the Wilcoxin-Signed rank test.

**Progress:** Investigators have performed initial analysis of results on 16 subjects, but have not yet performed statistical analysis. The protocol remains ongoing to complete analysis and final write up.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206105	<b>Status:</b> Ongoing
<b>Title:</b> Implementation of an Office-Based Screening Tool to Improve Adherence with Recommended Preventive Services in Primary Care		
<b>Principal Investigator:</b> COL Diane M. Flynn, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Gary W. Clark, MC; MAJ Ross E. Colt, MC; LTC Kathryn K. Ellis, MC; CPT Andrea S. Otto, MC; Janet O. Schertzer; John G. Meyer, MD		
<b>Start - Completion:</b> 7/5/2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if the use of a questionnaire and written instructions at every primary care visit to assess adherence with recommended preventive services will increase rates of recommended preventive services.

**Technical Approach:** Beginning 1 July 2006, all patients presenting for care at Madigan Family Medicine Clinics will be asked to complete a preventive services checklist to determine if they are up to date on recommended preventive services. The nurse or nursing assistant who screens the patient will assist the patient in completing the questionnaire as needed, will distribute appropriate educational materials as indicated and will order indicated labs and studies under the primary care provider's name. The provider who sees the patient will perform any indicated examination and order any indicated labs or studies as time permits. If time does not permit addressing preventive services, the patient will be instructed to make a follow up appointment for a periodic physical examination. Rates of adherence with recommended preventive services will be compared between the pre-intervention and post-intervention periods between patients seen in the Gold Team and those seen in other Family Medicine Clinic teams. Data will be prepared by the Health Outcomes section and will be devoid of patient identifiers.

**Progress:** This protocol began enrollment on 11 Sep 2006. Since that date, front desk clerks have been instructed to distribute the screening questionnaire to all adult patients who seek care on the Family Medicine Clinic Gold Team (exclusive of sick call patients).

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205130	<b>Status:</b> Ongoing
<b>Title:</b> Use of Pedometers Among Healthcare Providers in a Large Military Family Medicine Department		
<b>Principal Investigator:</b> CPT Kevin M. Kelly, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert C. Oh, MC; MAJ Alvin Y. Tiu, MC; LTC Telita Crosland, MC; CPT Jarret E. Sands, MC		
<b>Start - Completion:</b> 8/30/2005 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** To determine the affect of a pedometer exercise program on the level of physical activity of health care providers in a primary care clinic.

**Technical Approach:** This study sets out to determine the affect of a pedometer exercise program on the level of physical activity of health care providers in a primary care clinic. Residents, faculty, and mid-level providers in the MAMC Family Medicine Department, approximately seventy total subjects, will be enrolled in the study. Study subjects will be evaluated for baseline physical activity level category with the International Physical Activity Questionnaire (IPAQ) and baseline daily step count. They will be given a pedometer and instructions on increasing their daily activity level. Their daily step count will be followed for six weeks. The IPAQ will be repeated post intervention. A pre and post intervention BMI and blood pressure will be also measured. The change in number of steps taken per day, METS/day, and physical activity category (sedentary, low active, somewhat active, active, highly active) will be statistically analyzed correlated to independent variables of age, BMI, and blood pressure. Differences between staff, residents, and mid-level providers will also be evaluated.

**Progress:** This protocol closed to enrollment with 50 providers (subjects) enrolled. The subjects completed their six week pedometer course and returned their surveys and log books to the principal investigator. The information has been entered into a database; study staff is in the process of analyzing the data and writing up the project. No adverse events occurred. Anticipate study completion within the next two months.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206019	<b>Status:</b> Completed
<b>Title:</b> Pediatric Obesity in a Military Family Medicine Clinic		
<b>Principal Investigator:</b> LCDR Sandra L. Kimmer, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 11/28/2005 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The specific aims of this study is to measure the prevalence of pediatric obesity and overweight in children ages 6-11 enrolled at Madigan Army Medical Center Family Medicine Clinic and to discover the relationship between pediatric obesity in this population and race, sponsors active duty status, and socioeconomic status (SES) as measured by the sponsor's rank. An additional phase of this study is to determine the percentage of those children who meet criteria for obesity based on BMI for age that have not been formally diagnosed.

**Technical Approach:** ICDB records for all children who were age 6-11 and enrolled in the Madigan Army Medical Center Family Medicine Clinic during 2004 will be reviewed. Because age, sex, height, and weight are required to calculate the BMI percentile for age and sex and thus determine whether or not a child is obese, only those children who had a clinic visit in 2004 during which both height and weight were recorded will be selected for this study. If more than one visit meets these criteria, data from the most recent visit only will be used to calculate the BMI percent for age and sex.

**Progress:** This protocol was reported completed in July 2006. Excerpt of results:

Of the 668 subjects in the study cohort, 97 (14.5%) met the diagnostic criteria for obesity. An additional 92 (13.8%) children were clinically overweight. The mean BMI% for the overweight and obese children was 93.8% (SD=4.22). The average age for these children was 9.19 year (SD=1.67). The one-sample binomial test was used to compare the 14.5% obesity rate found in this study to the 15.3% rate reported among 6-11 year olds in the 1999-2000 NHANES study. These percentages were not significantly different ( $p=.307$ ). The prevalence of overweight (13.8%) was also not significantly different from the 1999-2000 NHANES prevalence of 15% ( $p=.202$ ).

The largest difference in weight status between the genders was seen in the overweight category. Of the overweight children, 58 (63.0%) were male and 34 (36.9%) were female. Overall, males had a 16.4% prevalence of overweight and a 14.7% prevalence of obesity. Female prevalence rates were 10.8% and 14.3% respectively. Chi-square analysis did not show a statistically significant difference in overweight or obesity based on gender ( $p=.102$ ). Almost 24% of 11 year olds in this study were clinically obese. Overweight was highest among 10 year olds with 18.8% of the cohort being clinically overweight. Increased age was the only independent variable to show a statistically significant relationship to weight status ( $p=.017$ ).

Of the 97 subjects who met the diagnostic criteria for obesity, only 12 had a formal diagnosis of obesity on their medical record. Only one of the 92 overweight children was formally diagnosed. This rate of diagnosis, 6.9% (13 out of 189 children), is significantly different from the 80% diagnosis rate, which was considered acceptable ( $p<.001$ ). The average BMI percentile for those children diagnosed (98.3%, SD=1.52) was similar for males was (98.4%, SD=0.98) and females (98.2%, SD=1.83). The mean BMI% for children diagnosed was higher than that of children who met criteria for overweight or obesity but were not diagnosed (93.8%, SD=4.22). This difference in BMI% was not statistically significant ( $p=.466$ ).

More females were diagnosed (10.1%) than males (4.5%) although this difference was not significant ( $p=.135$ ). The association between the type of provider seen and whether or not the overweight child was formally diagnosed approached significance ( $p=.076$ ). More nurse practitioners diagnosed overweight and obese children (16.1%) than physicians (7.8%) or physician's assistants (3.1%). The frequency of visits to a provider did not impact whether or not the diagnosis was made ( $p=.398$ ). Although health problems are common in overweight children, children in this cohort who met diagnostic criteria for overweight or obesity did not have significantly more visits than their normal weight peers ( $p=.276$ ).



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206048	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Controlled Trial of Manual/Manipulative Therapy for Acute Low Back Pain in Active Duty Military Personnel: A Pilot Study		
<b>Principal Investigator:</b> MAJ Douglas M. Maurer, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Scott T. Stoll, D.O., Ph.D.; MAJ Charles W. Webb, MC; CPT Jarret E. Sands, MC; CPT April E. Lynch, MC; CPT Richard J. Geshel, MC; MAJ David L. Brown, MC; CPT Hyrum F. Durtschi, MC; COL Gary W. Clark, MC; CPT Scott P Grogan, MC; Tonya N. Kozminski, MD		
<b>Start - Completion:</b> 3/21/2006 - Feb 2007	<b>Funding:</b> Samueli Institute for Information Biology	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate the efficacy of conservative, non-surgical, manually applied biomechanical treatments to reduce pain and improve function in young adult active duty military personnel with acute low back pain.

**Technical Approach:** This is a prospective, randomized, blinded, controlled clinical trial that plans to enrollment male and female Soldiers ages 18-25 consecutively from all military personnel presenting during sick call to the Acute Care Clinic, Department of Family Medicine, Madigan Army Medical Center, Fort Lewis, Washington. Informed consent will be obtained from the subjects who desire to participate in the study by the Clinical Research Coordinator (CRC) and assigned randomly to treatment (M/MT) or control (Standard Care) groups. The Study Evaluating Physician (SEP) will perform a routine exam to address the exclusion criteria. If the patient is not cleared for the study by the SEP s/he will enter routine care and be excluded from the study. If the subject is cleared for the study by the SEP, the subject will be given an appointment with a Study Treatment Provider (STP). The subject will be informed of the study group assignment and treatment initiated. All subjects will be scheduled to see the same STP for all study treatment visits. All subjects from both treatment and control groups will see the SEP for evaluation regarding modified duty assignment. The SEP and CRC will be blinded to group assignment. For this study, standard care will include prescribed medications including acetaminophen, ibuprofen or naprosyn, cyclobenzaprine for up to one week; acetaminophen with codeine for up to 1 week; passive modalities (ice, heat) for symptomatic relief; handouts on back self-care and exercises. Subjects will be reevaluated at 2 weeks and 4 weeks for improvement. The treatment group will receive manual/manipulative therapy (M/MT) in combination with standard care. M/MT involves a set of treatments with elements of both osteopathic manipulative and chiropractic techniques and sessions will be given up to twice a week for up to four weeks.

Pain will be measured using the Visual Analog Scale and quantification of medication use. Functionality will be assessed using the Roland Morris Questionnaire, Back Pain Functional Scale, and days on limited duty. Statistical analysis tools will include: descriptive statistics, cross tabulations and measures of association, chi-square for dichotomous variables, and a 2x3 mixed factorial ANOVA. Three one-way ANOVAs comparing the treatment groups on pain, functionality, medication use and other outcome scores will be performed using residualized improvement scores.

**Progress:** This protocol remains open to enrollment, with a total of 12 patients enrolled during FY06. All 12 patients received study treatment, but one patient failed to follow-up after the first visit and has had no further data collected. The remaining eleven patients continued to be followed. No adverse events have occurred. Enrollment will continue with the goal of 100 subjects completing the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205025	<b>Status:</b> Completed
<b>Title:</b> Prevalence of Vitamin B12 Deficiency in the Type 2 Diabetic Population		
<b>Principal Investigator:</b> CPT Matthew C. Pflipsen, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert C. Oh, MC; MAJ Aaron A. Saguil, MC; CPT Derek K. Seaquist, MC		
<b>Start - Completion:</b> 2/24/2005 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/4/2006

**Study Objective:** To determine the prevalence of B12 deficiency in Type 2 diabetics as documented by (1) B12 levels <100pg/ml or (2) B12 levels of 100-350pg/ml plus elevations in serum methylmalonic acid and homocysteine greater than 3 standard deviations above the mean of normal subjects.

**Technical Approach:** The study population will include 200 consecutive Type 2 diabetic patients older than 45 years of age presenting to the Family Medicine Clinic. Data on medication use, past medical history, and nutrition will be obtained by a survey. Blood samples will be collected for measurement of serum B12 levels. Measurement of serum methylmalonic acid and homocysteine will be carried out on samples requiring further testing for diagnosis. Descriptive statistics will be performed and associations between patients diagnosed with B12 deficiency and without B12 deficiency will be analyzed using the Chi-square test, Student t-test and multiple logistic regression.

**Progress:** This protocol completed data collection during FY06, with 204 subjects enrolled; 199 who completed study participation. The principal investigator has left MAMC; he reports that statistical analysis of the data remains ongoing. An abstract of findings was not available at the time of this report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206067	<b>Status:</b> Completed
<b>Title:</b> Determinants of Military Medical Student Interest in Family Medicine		
<b>Principal Investigator:</b> LTC Irene M. Rosen, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 3/27/2006 - Nov 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/30/2006

**Study Objective:** To determine the factors which influence military medical students' interest or lack of interest in the field of Family Medicine.

**Technical Approach:** A study questionnaire will be forwarded via electronic mail to all 3rd and 4th year medical students at the Uniformed Services University of the Health Sciences (USUHS) as well as those participating in the Health Professions Scholarship Program (HPSP). The study subjects will be asked for their cooperation with the questionnaire, informed that participation is completely anonymous and voluntary, and asked to email their responses back to the investigator who will collect and analyze all data.

**Progress:** Overall, 35 (11.3%) of survey respondents considered FM to be their specialty of choice at the time of survey administration. Twenty (57%) of these students named FM as a specialty they considered when entering medical school. The primary factors cited by students choosing FM were lifestyle and flexibility (71%), personality fit (65%), job satisfaction (65%), continuity of care (62%), diversity of patient population (59%), and the type of people who would be their future colleagues (59%). This is in interesting contrast to students choosing general surgery and surgical specialties, whose primary influencing factors were overall level of satisfaction (69%) frequency of deployments (54%), amount of specialty bonus (45%), and opportunity to sub-specialize (38%).  
**Conclusion:** This study shows that students choosing FM are motivated by different factors than students choosing other specialties, and we may influence student recruitment by focusing on the strengths of our specialty and highlighting these strengths during clinical rotations.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205103	<b>Status:</b> Completed
<b>Title:</b> The Role of Evidence and Other Determinants in Resident Discussions of Spirituality with Patients		
<b>Principal Investigator:</b> MAJ Aaron A. Saguil, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 10/17/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine which factors (including clinical evidence) are most likely to predict whether a family medicine resident is likely to initiate a discussion of a patient's spirituality. This study of family medicine residents seeks to (1) compare individual likelihood of initiating discussions of spirituality vis-à-vis discussions of medications, (2) compare the Spiritual Well-Being Scale (SWBS) scores (a validated surrogate for spirituality) of those more likely and those not more likely to initiate discussions of spirituality when given evidence linking spirituality with improved patient outcomes, and (3) analyze which demographic variables are significant predictors of likelihood of initiating discussions.

**Technical Approach:** A survey containing the SWBS and questions querying demographic and practice characteristics will be mailed to 750 family medicine residents (anticipated response rate 50%, or, 375 residents for  $\gamma = 0.80$  at a  $p < 0.05$ ). It will be mailed in three iterations to enhance response. Primary data collected will look at resident likelihood of initiating discussions of spirituality when presented with evidence linking spirituality with positive outcomes (which will be compared in an analytic fashion against resident likelihood of initiating discussions of a new medicine when presented with evidence linking the new medicine to positive outcomes); this data will be analyzed using the Wilcoxon Signed-Ranks Test. Data will also be collected on the mean SWBS score among those more likely and those not more likely to initiate spiritual discussions with patients; this data will be analyzed with Analysis of Variance (ANOVA) testing. Finally, the descriptive demographic data will be collected to see if any of these variables influence a family medicine resident's likelihood of initiating spiritual discussions; these data will be analyzed using multiple linear regression.

**Progress:** Results: Surveys from 385 of the 750 subjects were returned complete (51.3%). Twenty-two surveys were excluded; the adjusted response rate was 49.8%. The sample was 53.9% female. Approximately half of the respondents (48.9%) were over 30 years of age. Whites comprised 67.5% of the sample, and non-Christian religious affiliation represented 26.2%. Geographic regions were equally represented. Almost all residents (97.2%) said that they would discuss religion if requested to do so by a patient. The majority (71.3%) either 'strongly' or 'moderately' agreed that they would initiate discussions of spirituality more often if provided with good evidence that spirituality was associated with good health. Geographic region ( $p=0.004$ ), religion ( $p=0.005$ ), and SWBS quartile ( $p<0.001$ ), were significant, independent predictors of 'strongly' agreeing that one would be more likely to discuss spirituality. By subcategory, residents in the Northeast and Midwest were three times more likely to initiate discussion than those in the West. Protestants were almost four times more likely to do so than non-Christians. Residents in the lowest SWBS quartile were less likely to discuss spirituality than those in the highest quartile.

When directly compared to likelihood of discussing a new medication, 56% agreed that they would be at least as likely to discuss spirituality, given equal evidence for each. Region ( $p=0.002$ ), religion (0.002), and SWBS quartile ( $p<0.001$ ) continued to be significant, independent predictors of being as likely to discuss spirituality as a new medication. White respondents were less likely to discuss

spirituality than a medication, given equal evidence, than those in the 'Other' race category. Residents training in the Northeast and Midwest had higher odds ratios for being as likely to discuss spirituality as a medication than those in the West. Protestants and 'Other' Christians had higher odds ratios for being as likely to discuss spirituality as a medication than non-Christians. The average SWBS score for residents who were as likely to discuss spirituality as a medication was 102.6 (SD 14.3), compared to 92.3 (SD 16.5) for those who were not ( $p < 0.001$ ).

Conclusions: Family medicine residents are willing to discuss spirituality if requested by patients to do so. Additionally, given evidence, residents indicate that they are more likely to discuss spirituality than they do currently. However, given equally robust evidence for each, few residents indicated that they were as likely to start discussion of spirituality as they were a new medication. Additional investigations are needed to determine the barriers that prevent the acceptance of spirituality-related research.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206104	<b>Status:</b> Ongoing
<b>Title:</b> Implementing a Medical Ethics Curriculum in a Family Medicine Residency: Assessment of Need, Description of the Process, and Evaluation of Effectiveness		
<b>Principal Investigator:</b> LCDR Richard W. Sams, MC, USN		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Susan P. Opar, MC		
<b>Start - Completion:</b> 7/5/2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objectives are: (1) to assess family medicine residents and staff's baseline level of knowledge and comfort level in dealing with ethical issues in medicine, (2) to implement a medical ethics curriculum in the family medicine residency, describe the curriculum's content and implementation process and (3) to evaluate any gains in knowledge and comfort level from the educational intervention and participants' perceived value of the curriculum.

**Technical Approach:** All faculty and residents will be invited by email (Attachment #1) and announcements to participate in the study. They will be made aware that comparisons will be made of their LNA and post-test curricular survey. The numbered LNA tool will be placed in their mail boxes. They will be asked to return the completed tools to the associate investigator's mailbox. The curriculum will be implemented by integrating each 45 minute seminar into the already existing CME schedule. Four forty-five minute didactic sessions occur each Wednesday morning for CME and GME. Once per rotation block, a medical ethics seminar will be conducted by the PI during one of the four didactic sessions. The syllabus developed by the PI will serve as the template for the sessions. All members of the faculty and residents are encouraged to attend the CME lectures in general. At the one year mark the post-test curricular survey tool will be placed in all faculty and residents mailboxes, and they will be asked to complete the survey at that time. The post-test curricular surveys will have the same number for each person who completed the LNA. This information will then be analyzed. See the attached curriculum, which contains the syllabus, LNA and post-test / curricular survey.

The knowledge portion of the LNA and post-test consist of 10 multiple choice case-based questions, with one correct answer for each question. Each case has a corresponding question regarding how comfortable the person is with the described ethical dilemma and how to resolve it. The person is to respond by rating his or her level of comfort on a 10 point Likert scale. The LNA and post-test / curricular survey assesses the person's perceived value of the ethics training for preparing him or her to address similar ethical issues. This is assessed on a 10 point Likert scale. The LNA tool assesses how burdensome the LNA was to complete on a 10 point Likert scale. The post-test / curricular survey also assesses the following: participants perceived value of the curriculum personally and professionally; how many seminars were attended; and an assessment of was there too little, too much or the right amount of emphasis on medical ethics.

**Progress:** A total of 40 participants enrolled, which included family medicine staff and residents. Thirty of the 40 voluntarily and anonymously completed the learning needs assessment / pre-test. The data from this instrument is currently being analyzed. Four educational sessions were completed during the weekly continuing medical education time for the staff and residents.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205132	<b>Status:</b> Completed
<b>Title:</b> Colonoscopy by a Family Physician: A Case Series Demonstrating Healthcare Savings		
<b>Principal Investigator:</b> MAJ Matthew W. Short, MC		
<b>Department:</b> Family Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Kevin M. Kelly, MC		
<b>Start - Completion:</b> 9/1/2005 - Nov 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/22/2006

**Study Objective:** To illustrate the potential cost savings to the military health care system by implementing colonoscopy training in family medicine residency programs.

**Technical Approach:** A cost comparison/analysis will be done to show significant savings to the TRICARE system by implementing colonoscopy training in family medicine residency programs. Procedure reports will be reviewed on all 182 TRICARE beneficiaries receiving a colonoscopy at Bayne-Jones Army Community Hospital, Fort Polk, LA performed by a credentialed family physician between Sept 2003 and May 2005. Each procedure will be properly coded using the standard CPT code for the procedure, anesthesia, and pathology specimens. Standard E&M codes used by civilian gastroenterologists in the Louisiana community will also be included to determine the total cost. All reimbursable codes for each patient will then be multiplied by the actual cost billed to TRICARE in 2004 for the given procedures and outpatient visits. Data will show the total cost savings to the military health care system by utilizing a single family physician to perform colonoscopies one half day a week at Army community hospitals. Potential nation-wide yearly cost savings to TRICARE for civilian gastroenterology colonoscopy referrals will then be determined using the average colonoscopy cost and total number of civilian referrals in 2004 obtained from the Military Health System (MHS) Management Analysis and Reporting Tool.

**Progress:** This protocol was reported completed in August 2006. A chart review was conducted of all 182 colonoscopies performed by a FP at an ACH from September 2003 to May 2005. The total facility cost was \$52,632.34 (\$289.19 per colonoscopy). The total referral cost would have been \$156,197.60 (\$858.23 per colonoscopy). Utilizing a family physician saved the hospital \$103,565.26 (\$569.04 per colonoscopy). A family physician trained in colonoscopy saved significant healthcare dollars at an Army community hospital by decreasing civilian gastroenterology referrals. Note: the original title was 'Military Health System Cost Savings by Implementing Colonoscopy Training in Family Medicine Residency Programs.'

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205131	<b>Status:</b> Completed
<b>Title:</b> Esophagogastroduodenoscopy by a Family Physician: A Case Series Demonstrating Healthcare Savings		
<b>Principal Investigator:</b> MAJ Matthew W. Short, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Lloyd A. Runser, MC		
<b>Start - Completion:</b> 9/1/2005 - Nov 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/22/2006

**Study Objective:** To illustrate the potential cost savings to the military health care system by implementing esophagogastroduodenoscopy (EGD) training in family medicine residency programs.

**Technical Approach:** A cost comparison/analysis will be done to show significant savings to the TRICARE system by implementing diagnostic upper gastrointestinal endoscopy training in family medicine residency programs. Procedure reports will be reviewed on all 95 TRICARE beneficiaries receiving an EGD at Bayne-Jones Army Community Hospital, Fort Polk, LA performed by a credentialed family physician between Sept 2003 and May 2005. Each procedure will be properly coded using the standard CPT code for the procedure, anesthesia, and pathology specimens. Standard E&M codes used by civilian gastroenterologists in the Louisiana community will also be included to determine the total cost. All reimbursable codes for each patient will then be multiplied by the actual cost billed to TRICARE in 2004 for the given procedures and outpatient visits. Data will show the total cost savings to the military health care system by utilizing a single family physician to perform upper gastrointestinal endoscopies one half day a week at Army community hospitals. Potential nation-wide yearly cost savings to TRICARE for civilian gastroenterology EGD referrals will then be determined using the average EGD cost and total number of civilian referrals in 2004 obtained from the Military Health System (MHS) Management Analysis and Reporting Tool.

**Progress:** This protocol was reported completed in August 2006. A chart review was conducted of all 95 EGDs performed by a FP at an ACH from September 2003 to May 2005. The total facility cost was \$22,655.65 (\$238.48 per EGD). The total referral cost would have been \$55,614.95 (\$585.42 per EGD). Utilizing a family physician saved the hospital \$32,959.30 (\$346.94 per EGD). An endoscopy-trained family physician saved significant healthcare dollars at an Army community hospital by decreasing civilian gastroenterology referrals.



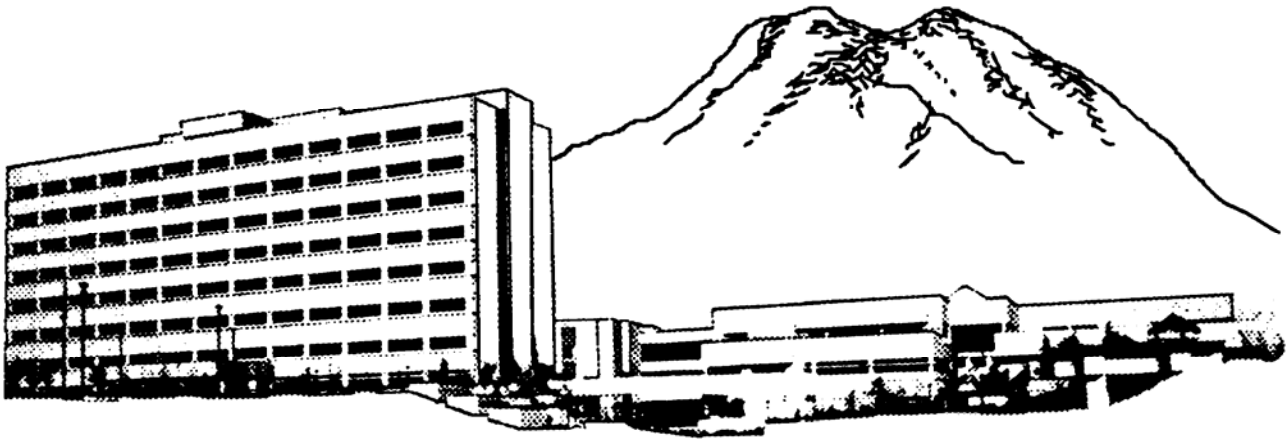
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206080	<b>Status:</b> Ongoing
<b>Title:</b> Predicting Intern Performance using an Objective Structured Clinical Examination		
<b>Principal Investigator:</b> MAJ Matthew W. Short, MC		
<b>Department:</b> Family Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert B. Blankenship, MC; MAJ Jennifer E. Jorgensen, MC; COL Bernard J. Roth, MC		
<b>Start - Completion:</b> 4/18/2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if intern performance on an Objective Structured Clinical Examination (OSCE) prior to internship is more predictive than prior academic performance in identifying potential deficiencies in Accreditation Council for Graduate Medical Education (ACGME) core competencies during the intern year.

**Technical Approach:** Sixty-one incoming clinical interns at Madigan Army Medical Center will complete an Objective Structured Clinical Examination (OSCE) during their intern orientation. This OSCE will evaluate each intern based on the Accreditation Council for Graduate Medical Education (ACGME) core competencies of patient care, medical knowledge, practice-based learning and improvement, interpersonal and communication skills, professionalism, and system-based practice. The objective of this study is to determine if intern performance on an OSCE prior to internship is more predictive than prior academic performance based on data from their First Year Graduate Medical Education (FYGME) application in identifying potential deficiencies in ACGME core competencies during the intern year. If the OSCE is more predictive of internship performance, deficiencies in ACGME core competencies identified during this examination could be remedied earlier to ensure successful completion of internship and result in more competent, caring physicians.

**Progress:** This is an educational protocol unrelated to patient care. A total of 61 new interns took the incoming Objective Structured Clinical Examination (OSCE), evaluating the six ACGME core competencies. All data from this initial exam has been compiled on a spreadsheet to be analyzed. Program directors' prediction of performance was also obtained prior to the exam and another progress report on the intern's performance will be obtained in January. The OSCE will be repeated at the end of the year, 5/6 June 2207, and the program directors' final evaluations of intern performance will be collected at that time.



# **Detail Summary Sheets**

## Graduate Medical Education

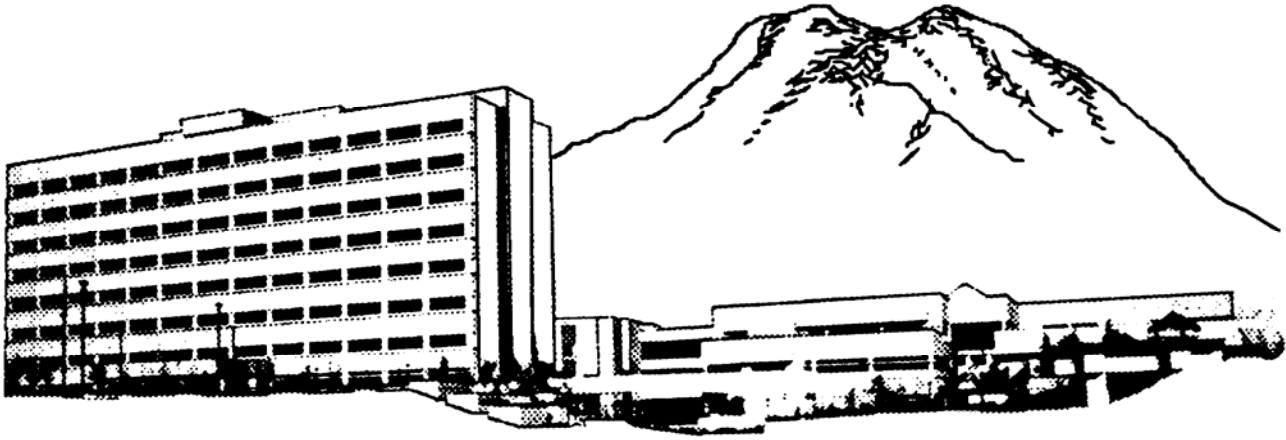
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205090	<b>Status:</b> Ongoing
<b>Title:</b> Attitudes and Perceptions of Refractive Surgery Among ROTC Cadets Presenting for a Flight Physical and Self-Reported Barriers Towards Having Refractive Surgery to Correct Visual Acuity and Becoming Medically Qualified for Army Aviation		
<b>Principal Investigator:</b> CPT John H. Boden, MC		
<b>Department:</b> GME	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ John A. Edwards, MC; LTC Mark L. Nelson, MC		
<b>Start - Completion:</b> 6/2/2005 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** To identify attitudes and perceptions ROTC cadets applying for Army aviation have towards refractive surgery. This protocol will also attempt to identify any perceived barriers to receiving an exception to policy after having refractive surgery.

**Technical Approach:** This study will identify attitudes, and perceptions ROTC cadets have towards refractive surgery, in addition to identifying any perceived barriers cadets might have towards receiving an exception to policy after having refractive surgery. The study will include ROTC cadets who will undergo a flight physical medical examination in the year 2005. The sample population size will be approximately 600 ROTC cadets. Cadets will answer simple questions on a questionnaire given to them prior to having their flight physical. Analysis of answers provided on questionnaires will include correlation between subjects understanding of Army policy on refractive surgery, level of interest in becoming branch aviators, and understanding of the process entailed in receiving an exception to policy after having refractive surgery.

**Progress:** This protocol remains ongoing. A total of approximately 640 cadets applying for flight status during warrior forge 2005 completed the study questionnaire. Data from the questionnaires has been tabulated and data analysis is currently being worked on.



## Detail Summary Sheets

Health Outcomes Management Division

## Detail Summary Sheet

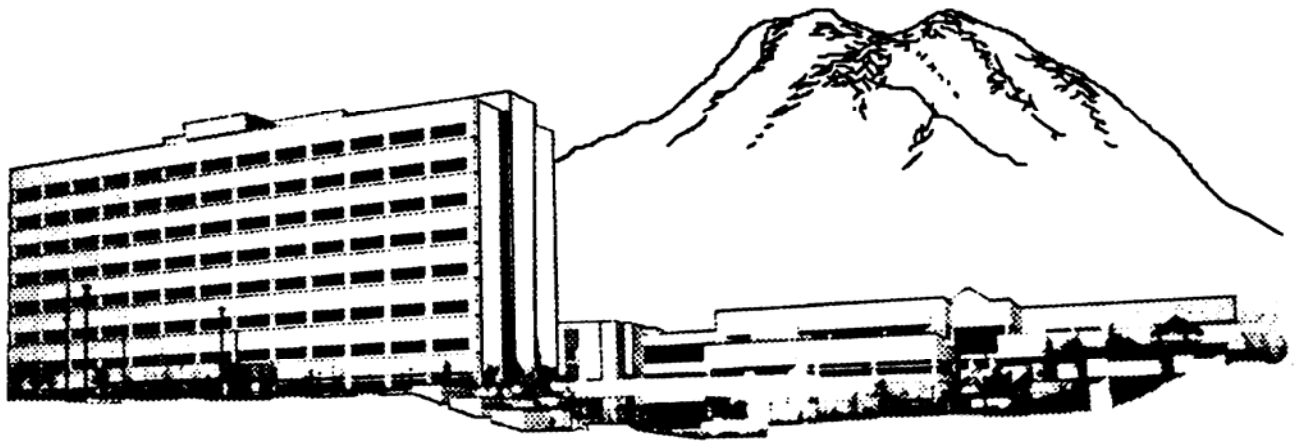
<b>Date:</b> 30 Sep 06	<b>Number:</b> 205108	<b>Status:</b> Ongoing
<b>Title:</b> The Deployment of Physical Therapy for Combat: A Description of the Process and Outcomes		
<b>Principal Investigator:</b> John G. Meyer, MD		
<b>Department:</b> Outcomes	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Mona O. Bingham, AN; MAJ Daniel M. Jayne, MC; CPT Brian W. Jovag, MC		
<b>Start - Completion:</b> 7/21/2005 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/29/2006

**Study Objective:** The overall goal of this study is to describe injuries and the impact of providing physical therapy evaluation and treatment intervention prior to and during combat deployment for a brigade (BDE) of soldiers. There are 5 specific aims to meet this overall goal. Using data already collected from computerized medical records and hospital information systems, the aims of this secondary data analysis study are: (1) Describe a BDE of soldiers anticipating immediate deployment and specifically those with physical orthopedic complaints and injuries. (2) Describe the impact of pre-deploying screening and intervention for orthopedic complaints in a deploying BDE. (3) Compare orthopedic health and injuries of soldiers in an AD BDE versus soldiers in an Army National Guard (ARNG) BDE. (4) Describe the impact of physical therapy care provided in the field environment for a combat BDE during a combat deployment. (5) Compare pre-deployment Health Risk Assessment II (HRA II) results to post-deployment HRA II results.

**Technical Approach:** For this retrospective study, data will be obtained from the computerized medical records available at Madigan Army Medical Center (MAMC) and other health information system collected as part of the SRP. The population of soldiers assigned to the 81st BDE and the 3rd BDE (and additional units who provided support or were supported by the BDEs during this deployment) who completed the Soldier Readiness Process (SRP) prior to deployment, immediately post deployment, and 90-days post deployment will be examined to meet the study goals. This number is anticipated to be no more than 75% of the BDEs. However descriptive data from the SRP process on the Health Risk Appraisal II (HRA II) of both BDEs will be collected to adequately describe the differences and similarities between the 2 BDEs. Data will be collected on a number of outcome variables including: demographic data, and number of soldiers in BDE who self-reported pain, made PT self-referrals, SRP PT referrals, returned via Medical evacuation, seen for healthcare in theater by PT and other PCP. Other outcome variables include: lost work time, medical convoy hours, number of PT treatment procedures, number of injuries, type of injury/diagnosis, time soldier not able to perform combat mission, number of follow-up physical therapy visits, profile type and length, pain level as determined by physical therapist, final disposition, and HRA II limited activity answers.

The analysis plan includes a number of different analysis techniques to answer the research questions/objectives. SPSS will be used to run all descriptive statistics (means, standard deviations, percentages). To compare orthopedic health and injuries of soldiers in an AD BDE versus soldiers in an Army National Guard BDE], Chi-square will be used for categorical variables and either T-tests or Mann-Whitney U tests for measured variables to determine relationships. ANOVA will be used to determine relationships for interval data. To compare pre-deployment Health Risk Assessment II (HRA II) results to post-deployment HRA II results], Chi-square will be used for categorical variables and either T-tests or Mann-Whitney U tests for measured variables to determine relationships. ANOVA Repeated Measures will be used to determine relationships for interval data with multiple time points (multiple medical visits/injuries) and Cochran Q.

**Progress:** Initiation of this protocol was significantly delayed due to PCS moves of two study investigators. This study will resume data analysis during FY07.



## **Detail Summary Sheets**

Cardiology Service, Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202300	<b>Status:</b> Ongoing
<b>Title:</b> CardioSEAL Septal Occlusion System (HUD)		
<b>Principal Investigator:</b> COL David T. Schachter, MC		
<b>Department:</b> Medicine/Cardiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 3/11/2002 - Dec 2004	<b>Funding:</b> Nitinol Med Tech via HDE	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** Humanitarian Use Device

**Technical Approach:** The CardioSEAL Septal Occlusion System is approved as an HUD for the indication of patent foramen oval closure (PFO). MAMC investigators trained to deploy this device must submit certificates of training and updated curriculum vitae to the Chairman, IRB. Use of the device will be tracked per 21 CFR 814.124(a).

**Progress:** Nine patients have undergone successful implantation of the CardioSEAL device without complications, one during FY06. All patients had strokes/TIA and evidence of PFO by bubble study. No further stroke/TIA events have been detected in any of the nine patients.



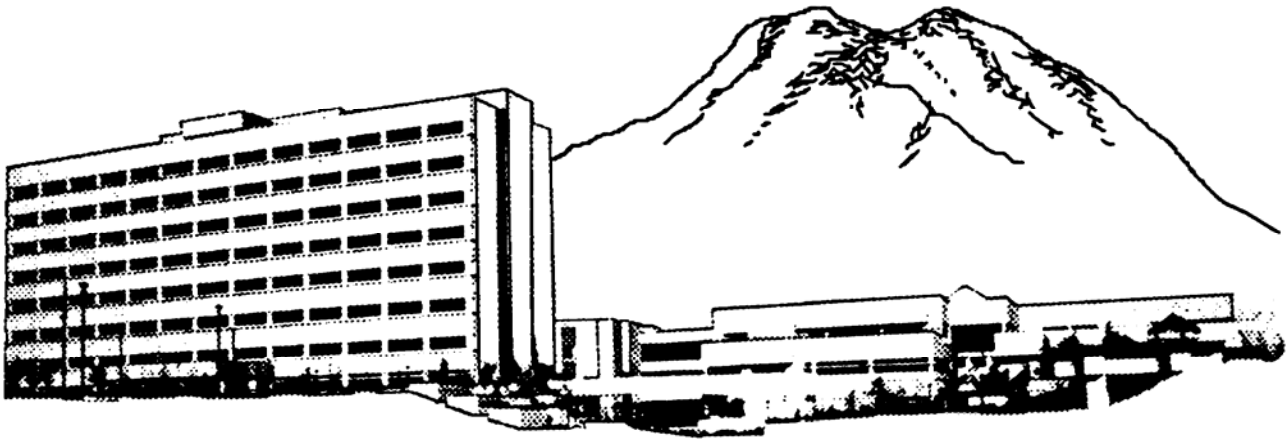
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201300	<b>Status:</b> Ongoing
<b>Title:</b> Jostent Coronary Stent Graft (HUD)		
<b>Principal Investigator:</b> COL David T. Schachter, MC		
<b>Department:</b> Medicine/Cardiology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Bruce R. Kenwood, MC		
<b>Start - Completion:</b> 9/25/2001 - Sep 2010	<b>Funding:</b> Jomed via HDE	<b>Periodic Review:</b> 8/28/2006

**Study Objective:** Humanitarian Use Device

**Technical Approach:** The Jostent Coronary Stent Graft is approved as an HUD for the indication of arterial perforation. Physicians trained to deploy the stent will be added as associate investigators upon receipt of documentation of training. Use of the device will be tracked per 21 CFR 814.124(a).

**Progress:** This Humanitarian Use Device was not utilized during FY06. A Jostent device was inserted in a patient for a perforated saphenous vein graft in April 2005. The patient is doing well and continues to be followed.



## **Detail Summary Sheets**

Hematology/Oncology Service, Department  
of Medicine

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206113	<b>Status:</b> Ongoing
<b>Title:</b> CTSU E5202: A Randomized Phase III Study Comparing 5-FU, Leucovorin and Oxaliplatin versus 5-FU, Leucovorin, Oxaliplatin and Bevacizumab in Patients with Stage II Colon Cancer at High Risk for Recurrence to Determine Prospectively the Prognostic Value of Molecular Markers		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 11/28/2006 - Aug 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to demonstrate an improvement in 3-year disease-free survival for high risk stage II colon cancer patients randomly assigned to 5-FU, leucovorin, and oxaliplatin (FOLFOX) versus FOLFOX plus bevacizumab.

Secondary objectives of this study are to: Compare overall survival between regimens; further identify the toxicities of the regimens; prospectively determine the impact of tumor biological characteristics on the survival of patients with stage II colon cancer.

**Technical Approach:** In this study, patients determined to be high-risk by the molecular analysis will receive chemotherapy +/- bevacizumab. A total of 3610 patients will be enrolled in this study, with up to 10 patients per year enrolled at MAMC. Baseline assessment will include history and physical, vitals and performance status, CBC, Chemistry, LFTs, CEA, PT, PTT, INR, urine protein/creatinine (UPC) ratio, and serum pregnancy test if applicable. All eligible, consenting participants will have a block of resected tumor sent to a central lab for biology-based risk assessment. Patients found to be low risk, will be registered to Arm C, the observation arm. Patients found to be high risk, will be randomized to receive either: ARM A (control arm): 5-FU, leucovorin, and oxaliplatin (FOLFOX regimen) IV every 2 weeks x 12 or ARM B: FOLFOX plus bevacizumab IV every 2 weeks x 12, followed by bevacizumab alone for 12 additional treatments (IV every 2 weeks). Patients will be followed every 3 months for 2 years, every 6 months for Year 3 through Year 5, and then every 12 months thereafter for a total of 10 years. Follow-up will include physical exam, performance status, CEA, and colonoscopy and biopsy where indicated.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 25 July 2006. PI response to CIRO review remains pending at the time of this report.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206023	<b>Status:</b> Ongoing
<b>Title:</b> A Multi-Center, Randomized, Phase 3 Study of Iodine I-131 Tositumomab Therapeutic Regimen Versus Ibritumomab Tiuxetan Therapeutic Regimen for Subjects with Relapsed or Transformed Follicular Non-Hodgkin's Lymphoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Antonio G. Balingit, MC; Jane E. Besich-Carter, BS, BCNP		
<b>Start - Completion:</b> 4/13/2006 - Jan 2011	<b>Funding:</b> GlaxoSmithKline via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** This study will compare the proportion of subjects treated with Iodine I 131 tositumomab therapeutic regimen who experience any Grade 3/4 hematological adverse event with the proportion of subjects treated with ibritumomab tiuxetan therapeutic regimen who experience this type of adverse event. Subjects in this study must have had at least three prior therapies for either follicular non-Hodgkin's Lymphoma (NHL) or follicular NHL that has transformed to diffuse large cell lymphoma.

The secondary objectives for efficacy are comparison of the confirmed overall response rate, confirmed complete response rate, and duration of response, as well as event-free survival, progression free survival, time to next treatment, and overall survival between the two treatment groups. Establishment of the non-inferiority of Iodine I 131 tositumomab compared to ibritumomab tiuxetan based on event-free survival will be the principal secondary objective.

The secondary safety objectives are safety comparisons between the Iodine I 131 tositumomab and ibritumomab tiuxetan treatment groups for the following events: Infusional toxicities (all and Grade 3/4), Gastrointestinal toxicities (all and Grade 3/4), Immune response (Human Anti-Murine Antibody [HAMA]), Elevated thyroid-stimulating hormone (TSH), Myelodysplastic syndrome (MDS)/acute myelogenous leukemia (AML), Serious adverse events (SAEs) related to cytopenia (bleeding events, neutropenic, fever, infections, hospitalization for hematologic supportive care). To characterize the safety profile in the two treatment groups, including the frequency of adverse events, the duration of infusion, and tolerance of first subsequent NHL therapy. To summarize safety and efficacy outcomes during the first subsequent treatment encounter for NHL. To establish the non-inferiority of confirmed overall response rates and confirmed complete response rates between Iodine I 131 tositumomab and ibritumomab tiuxetan.

**Technical Approach:** This is a randomized, multi-center, Phase III study comparing I131 tositumomab (Bexxar) versus Y90 ibritumomab tiuxetan (Zevalin) in subjects with relapsed or transformed follicular non-Hodgkin's lymphoma who have received prior treatment with rituximab (Rituxan). A total of 350 subjects will be randomized into two treatment arms, with up to 10 subjects being enrolled at MAMC. Subjects will be randomly assigned to one of the two treatment arms. Randomization will be stratified by baseline bone marrow involvement, baseline blood count and prior fludarabine treatment and conducted separately within each stratum. Subjects on Arm A will be treated with the standard Zevalin regimen, including rituximab and radiolabeled ibritumomab tiuxetan in two separate doses for imaging and therapy. Subjects randomized to Arm B will be treated with the standard Bexxar regimen in two separate doses for imaging and therapy. Subjects in each arm will be followed for ten years after receiving study drug (five years for efficacy endpoints and ten years for safety endpoints). After study drug administration, labs will be drawn at least weekly for up to 13 weeks to closely monitor hematological toxicity.

Response assessments will be done at Weeks 7, 13, 26, 39 and 52 during the first year, every six months during the second year, then annually through five years or until first subsequent treatment. See schema, protocol page 22. The study is powered to detect a significant reduction of 15% in Grade 3/4 hematologic toxicity. In addition, the study will have 90% power to establish non-inferiority of the Bexxar treatment versus Zevalin.

**Progress:** This protocol remains open to patient entry, with no subjects screened or enrolled during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205094	<b>Status:</b> Terminated
<b>Title:</b> A Randomized, Open-Label Trial Comparing Two Avastin™ (Bevacizumab)-Based Treatment Regimens For The First-Line Treatment Of Metastatic Colorectal Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 12/15/2005 - Aug 2010	<b>Funding:</b> Genentech via Henry M. Jackson Foundation	<b>Periodic Review:</b> 6/28/2006

**Study Objective:** To compare the efficacy, as measured by progression-free survival (PFS), of FOLFOX/Avastin followed by FOLFIRI/Avastin versus FOLFAX/Avastin followed by 5-FU/LV/Avastin as first-line therapy for previously untreated metastatic colorectal cancer. Secondary Objectives: (1) to evaluate the efficacy, as measured by overall survival, of FOLFOX/Avastin followed by FOLFIRI/Avastin versus FOLFOX/Avastin followed by 5-FU/LV/Avastin as first-line therapy for previously untreated metastatic colorectal cancer (2) to evaluate the tolerability of sequential treatment in subjects during first-line therapy, as measured by time to first-line treatment response (3) to evaluate the safety of an Irinotecan/Avastin-based regimen versus 5-FU/Avastin regimen following abbreviated FOLFOX/Avastin as first-line therapy for previously untreated metastatic colorectal cancer, as measured by the incidence of serious adverse events, selected adverse events, and treatment discontinuation for reasons other than tumor progression.

**Technical Approach:** This is a randomized, open-label trial comparing two Avastin (bevacizumab) based treatment regimens for the first-line treatment of metastatic colorectal cancer. Subjects who qualify will be randomized to one of two treatment arms. Subjects in both treatment arms will receive FLOFAX/Avastin every 2 weeks for eight cycles. At the end of the first eight cycles, subjects who have not experienced disease progression will receive treatment as follows: Arm A subjects will receive FLOFAX/Avastin every 2 weeks until disease progression or unacceptable toxicity, at which point they will be discontinued from the study. Arm B subjects will receive 5-FU/LV/Avastin every 2 weeks until disease progression or unacceptable toxicity, at which point they will be discontinued from the study. All subjects who have documented disease progression will be discontinued from the study. Subjects will be followed for adverse events for 30 days after the last dose of study treatment or subject discontinuation. Subjects will be followed for survival and post-progression therapy every 3 months until death, withdrawal of consent, or termination of the study by Genentech.

Post-progression therapy will not be specified by protocol. It is recommended that as initial post-progression therapy, subjects in Arm A receive FOLFOX re-induction if feasible and that subjects in Arm B receive Irinotecan-based therapy. In conjunction with post-progression therapy, subjects can receive biological therapy with Avastin and/or Cetuximab at the physician's discretion. Subjects will be monitored during the entire treatment phase and will be followed as appropriate. Subjects who are discontinued from treatment for any reason will be evaluated 30 days after the decision to discontinue study treatment.

**Progress:** This protocol was terminated by the Study Sponsor due to slower than expected accrual and an unexpected high rate of early discontinuation from study treatment for reasons not related to toxicity. No MAMC subjects were screened, consented or enrolled. There are no unreported IND safety reports at this time.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206103	<b>Status:</b> Terminated
<b>Title:</b> Phase 3, Multicenter, Multi-National, Open-Label Study to Evaluate the Safety and Efficacy of Alfimeprase in Subjects with Occluded Central Venous Access Devices		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> Never approved	<b>Funding:</b> Nuvelo, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate the safety profile of alfimeprase assessed by monitoring of adverse events and major bleeding events for up to 120 minutes following the final instillation of alfimeprase. To evaluate the efficacy of alfimeprase measured by the proportion of subjects with re-establishment of a functional CVAD at 15 minutes following the initial instillation of study drug, 30 minutes following the initial instillation of study drug and 30 minutes following the instillation of one or two doses of study drug.

**Technical Approach:** This a Phase 3, multicenter, multinational, open label trial to assess the safety and efficacy of intra-luminal alfimeprase 3.0 mg in subjects with occluded central venous access devices (CVAD). A total of 800 subjects will be enrolled and up to 20 at MAMC. Patients with single lumen, multilumen, centrally inserted, peripherally inserted and implanted ports that are occluded will be enrolled. They will receive intra-luminal alfimeprase (2ml) and it will be left in the catheter for up to 30 minutes. Re-establishment of catheter function will be assessed by an attempt to draw 3mL of blood and infuse 5mL saline at 5, 10, 15, and 30 minutes of first dose. If patency of the catheter is not restored after 30 minutes of first dose of the drug then a second dose will be administered and left in the catheter for an additional 30 minutes. Safety will be assessed by monitoring serious adverse events, adverse events and major bleeding events for up to 120 minutes after instillation of the final dose of the drug. Vital signs, venous blood for laboratory testing will be collected at 8 to 24 hours after instillation of the first study drug dose. After the study period which could be up to an hour the patients will be followed-up at 2 hours after instillation of the final study drug dose. Again at 8-24 hours and 28-45 days after instillation of the first study drug dose. The proportion of patients with re-establishment of functional CVAD at 15 minutes following the instillation of the study drug will be the major efficacy end point.

**Progress:** This protocol was terminated 27 September 2006, prior to final approval due to failed contract negotiations with the study sponsor. The study was never initiated at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205007	<b>Status:</b> Suspended
<b>Title:</b> PSOC 2003: A Phase II Study Evaluating the Efficacy of Gemcitabine, Carboplatin, Dexamethasone and Rituximab for Previously Treated Lymphoid Malignancies, UW Protocol Number LYM.03.01		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 2/18/2005 - Oct 2009	<b>Funding:</b> NCI via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10/24/2006

**Study Objective:** (1) To determine the feasibility and safety of Gemcitabine/Carboplatin/Dexamethasone with or without Rituximab in previously treated lymphoid malignancies. The primary end-point will be response rate (Rituximab will only be evaluated in CD20 positive malignancies). (2) To determine the efficacy of the above regimen. (3) To determine the ability to proceed to blood stem peripheral blood collection following the above regimens the impact of above regimen on stem cell reserve. (4) To determine remission duration.

**Technical Approach:** PSOC 2003 is a multicenter single arm phase II trial of Gemcitabine, Carboplatin, and Dexamethasone in the treatment of recurrent or refractory lymphoma (including B-cell, T-cell, and Hodgkin's disease). Patients with CD20 positive B-cell lymphoma will also be treated with Rituximab. The end points of the trial include response rate, duration of remission, and the ability to collect stem cells for possible future autologous stem cell transplant. The goal accrual of the study is 51 patients over 2 to 3 years. We anticipate accruing two patients per year at Madigan. The study will be monitored for accrual, adverse events and patient deaths every 6 months by the Study Investigator, Dr Ajay Gopal of the University of Washington and the Fred Hutchinson Cancer Research Center, and will be monitored annually by the Fred Hutchinson Cancer Research Center Protocol Data Monitoring Committee.

**Progress:** This protocol remains open to enrollment with one patient enrolled at MAMC who continued to be followed during FY06.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 89080	<b>Status:</b> Terminated
<b>Title:</b> SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast Cancer Having Involved Axillary Nodes and Positive Hormone Receptors		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10/20/1989 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/14/2006

**Study Objective:** To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term Tamoxifen or with chemoendocrine therapy with CAF, followed by long-term Tamoxifen or with concurrent chemoendocrine therapy with Tamoxifen and CAF and to compare the relative toxicity of the three therapies.

**Technical Approach:** Tumors must be pathologic stage T1, T2, or T3; N; MO (Stage II or selected Stage IIIA). Patients must have histologically proven adenocarcinoma of the breast with at least one positive lymph node (tumor and/or nodes must not be fixed). Patients must have undergone a radical, modified radical, or breast sparing procedure plus axillary dissection (level I or level II). Patients with bilateral breast cancer are ineligible. Estrogen and progesterone receptors must be assayed and one and/ or the other must be positive by the institutional laboratory standards of >10 fmol/mg protein. Prestudy studies must reveal no evidence of metastatic disease. Prior hormonal or chemotherapy is not allowed and prior postmenopausal estrogen therapy is allowed but must be discontinued before registration. Stratification factors will include: involved nodes (1-3, >4); PgR+ (ER positive or negative) vs PgR(ER positive); time from surgery to randomization (<6 vs >6 weeks). Patients will be randomized to one of three treatment arms: Arm I: Tamoxifen x 5 years, Arm II: Intermittent CAF x 6 courses followed by Tamoxifen x 5 years, Arm III: Intermittent CAF x 6 courses with concurrent Tamoxifen x 5 years.

**Progress:** This protocol closed to patient entry in August 1995, with six patients enrolled at MAMC; three who remained in long-term follow-up. The protocol was terminated during FY06 and the three surviving patients will continue to be followed under MAMC #99019, SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 90027	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor- Positive Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 2/16/1990 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 12/4/2006

**Study Objective:** To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

**Technical Approach:** Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years. Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

**Progress:** This protocol closed to patient entry in February 1994, with 6 patients enrolled. Three patients are deceased and three remain disease free and continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 90029	<b>Status:</b> Terminated
<b>Title:</b> SWOG 8897 (EST-2188, CALGB-8897, INT-0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History Follow-up Study in Low-Risk, Node Negative Patients		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 1/19/1990 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 12/1/2005
<b>Study Objective:</b> To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.		
<b>Technical Approach:</b> Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.		
<b>Progress:</b> This protocol closed to patient entry in January 1993, with six patients enrolled at MAMC who remain disease free. The protocol was terminated during FY06 and the six surviving patients will continue to be followed under MAMC #99019, SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 90056	<b>Status:</b> Completed
<b>Title:</b> SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 4/20/1990 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2/8/2006

**Study Objective:** To determine the objective response rate and duration of remission of BEP compared to VIP combination chemotherapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; to confirm the efficacy and toxicity of intravenous Mesna as a urothelial protective agent.

**Technical Approach:** Patients must have a histologic diagnosis of advanced disseminated germ cell tumor and no prior chemotherapy or radiation therapy. Patients will be randomized to VIP (cisplatin, ifosfamide, mesna, and etoposide) to BEP (cisplatin, etoposide, and bleomycin). The regimen will be repeated every three weeks for four cycles. Bleomycin will be omitted for postsurgery chemotherapy in BEP patients. Patients in complete remission at the end of four courses of therapy will receive no further treatment. If there is radiographic or serologic evidence of persistent disease and residual tumor is surgically resectable, surgery will be performed. Patients who have complete or near complete resection of residual radiographic abnormalities with the pathologic finding of fibrosis/necrosis and those who have complete resection of mature or immature teratoma will receive no further treatment. Patients who have complete resection of residual disease which histologically shows viable carcinoma will receive two more courses of the original induction therapy. If residual tumor is deemed unresectable, patients will be followed monthly until disease progression with no further therapy. If relapse occurs in complete or partial responders less than 4 weeks after day 1 of the last course of induction therapy, the patient will be taken off study.

**Progress:** This protocol closed to patient entry in April 1992, with one patient enrolled. The protocol was reported completed during FY06 when long-term follow-up data was no longer required on the surviving patient.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 97096	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9059 (E1392, INT-0126): Phase III Comparison of Standard Radiotherapy versus Radiotherapy plus Simultaneous Cisplatin, versus, split-Course Radiotherapy plus Simultaneous Cisplatin and 5-Fluorouracil, in Patients with Unresectable Squamous Cell Carcinoma of the Head and Neck		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 5/16/1997 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/10/2006

**Study Objective:** 1) To compare the effectiveness of standard radiation therapy alone to radiation therapy and simultaneous chemotherapy with cisplatin to split-course radiation therapy with cisplatin and 5-fluorouracil infusion in patients with unresectable Stage III and IV squamous cell carcinoma of the head and neck. Endpoints will include complete response rate, time to treatment failure, and overall survival. 2) To compare the relative toxicities of these treatment arms, in this patient population. 3) To compare patterns of relapse or treatment failure among these regimens. 4) To further assess the role, timing, and success of surgery in patients achieving a response to non-operative therapy.

**Technical Approach:** Unresectable Squamous Cell Carcinoma has a dismal prognosis with 3 year survivals in the 25' range. Several studies have shown that adding chemotherapy to radiation therapy may improve response rates and may allow some patients to get surgery after therapy. There are two approaches to adding chemotherapy to radiation therapy. One way is to give concurrent therapy with Cisplatin alone with combined continuous radiation therapy (Al Sarraf regimen) or to give combination Cisplatin and 5-FU with split course (Adelstein Regimen). These two regimens have met with some success in single ARM Phase II studies and have resulted in some patients having subsequent surgeries translating into longer survivals. It is thus the aim of this study to evaluate efficacy of three different regimens with continuous radiation therapy alone serving as the third ARM. Toxicities from these regimens are reasonable.

**Progress:** This protocol closed to patient entry in April 2000, with two patients enrolled. One patient died of progressive disease and the other patient remains disease free and continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 93032	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9061 (EST-2190, INT 0121): A Phase III Study of Conventional Adjuvant Chemotherapy vs High Dose Chemotherapy and Autologous Bone Marrow Transplantation or Stem Cell Transplantation as Adjuvant Intensification Therapy Following Conventional Adjuvant Chemotherapy in Patients with Stage II and III Breast Cancer at High Risk of Recurrence		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10/7/1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10/31/2006

**Study Objective:** To compare the sites and rates of recurrence, disease-free survival and overall survival, and toxicity of adjuvant chemotherapy (CAF) with adjuvant chemotherapy plus high-dose therapy with cyclophosphamide and the TEPA with autologous marrow infusion in patients with breast cancer with 10 or more positive lymph nodes.

**Technical Approach:** Patients will be stratified according to estrogen receptor status, age, and menopausal status and then randomized to receive radiotherapy plus tamoxifen or high-dose chemotherapy and autologous bone marrow transplantation. Both arms will receive cyclophosphamide 100 mg/m<sup>2</sup> PO X 14 days, doxorubicin 30 mg/m<sup>2</sup> IV days 1 & 8, and flurouracil 500 mg/m<sup>2</sup> IV days 1 & 8 repeated every 28 days x 6 cycles (CAF). Patients receiving CAF without bone marrow transplantation will begin radiation therapy within 4 weeks of the last dose of chemotherapy or when the WBC > 2900 and Platelets > 100,000. Patients randomized to receive high-dose chemotherapy will have bone marrow harvested no sooner than 4 weeks nor longer than 8 weeks after the last previous dose of myelotoxic chemotherapy. The CBC must be normal and the bone marrow normocellular and free of tumor by bilateral iliac crest biopsy within 4 weeks prior to storage. After the bone marrow is harvested, high-dose chemotherapy of cyclophosphamide 6000 mg/m<sup>2</sup>/96 hr and ThioTEPA 800 mg/m<sup>2</sup>/96 hr (4 days), will be given by continuous infusion over 4 days, days -6 to -2. Autologous bone marrow reinfusion will be on day 0. Patients receiving BMT will again be randomized to receive GM-CSF as a daily 2, 6 or 24 hour intravenous infusion beginning 2-4 hours after bone marrow infusion. GM-CSF will be initiated at a dose of 250 mcg/m<sup>2</sup>/d. Treatment will continue until the patient has achieved an absolute neutrophil count (ANC) of = 1000 cells/ul on 3 consecutive days or a planned duration of 28 days of treatment.

Tamoxifen 20 mg PO q.d. will be given to all patients who are estrogen or progesterone receptor positive after the completion of all chemotherapy for 5 years. For patients not randomized to receive transplant, Tamoxifen should be initiated 28 days after the start of the last CAF cycle. Patients randomized to receive transplant should begin Tamoxifen following transplant when WBC > 4000 and/or ANC > 2000. Patients will be taken off-study if there is development of metastatic disease at any time while therapy is ongoing. Measurement of effect is recurrence, disease-free survival or survival (survival is measured from the date of randomization to date of death). At measured times during the study a Breast Chemotherapy Questionnaire (BCQ) will be completed to separately document the changes in psychosocial function that occur on the two regimens. Not all subjects will complete the questionnaire at all time points, but if at least 150 per arm have complete data, the width of a 95% confidence interval on the mean change in scores would be about  $\pm 0.09$ . The BCQ will also be used to make comparisons between regimens. A 2 degree of freedom test based on the difference of the means of the 36 week evaluation and the difference of the means of the 52 week evaluation will be used.

**Progress:** This protocol closed to patient entry in August 1998, with one patient enrolled who remains disease free and continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 93097	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9205: Central Prostate Cancer Serum Repository Protocol		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 5/7/1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/10/2006

**Study Objective:** 1) To store serum of patients with confirmed adenocarcinoma of the prostate entered onto clinical trials conducted by the SWOG Genitourinary Committee. 2) To provide the serum of the above patients entered onto SWOG studies for specific clinical-laboratory investigations outlined on separate SWOG protocols approved by the Genitourinary Committee Tumor Biology Subcommittee.

**Technical Approach:** This serum bank is to provide the opportunity for study of new or existing markers or other tests in a prospective or retrospective fashion, in order to test their usefulness as diagnostic or management tools in prostate cancer at all stages. Specific information regarding the nature of individual tests to be conducted on the serum samples of these patients will be described in individual protocols. All serum samples (approx. 3 - 5 cc) will be collected from patients in the frequency and timing indicated on specific protocols. Samples will be spun 15 minutes after collection and stored at a minimum of -20°C. Samples will be frozen and shipped to the Serum Bank Coordinator.

**Progress:** This prostate cancer companion protocol remains open to enrollment with 14 patients enrolled at MAMC, two during FY06.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 93136	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9221, MDACC ID 91-025, INT-191-001: Phase III Double-Blind Randomized Trial of 13-Cis Retinoic Acid (13-cRA) to Prevent Second Primary Tumors (SPTs) in Stage I Non-Small Cell Lung Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 7/2/1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/24/2006

**Study Objective:** To evaluate: (1) the efficacy of 13-cis-retinoic acid (13-cRA) in reducing the incidence of SPTs in patients who have been treated for Stage I non-small cell lung cancer with complete surgical resection; (2) the qualitative and quantitative toxicity of 13-cRA in a daily administration schedule; and (3) compare the overall survival of patients treated with 13-cRA vs. patients treated with placebo.

**Technical Approach:** Patients enrolling into this study will be stratified according to histology, T stage and smoking status then registered into a Single-Blind, 8 week run-in period to test compliance. All patients will receive placebo during this period. After Run-in the patients will be randomized into a double-blind trial to receive 13-cRA (30 mg p.o./d x 3 yrs vs. Placebo (30 mg p.o./d x 3 yrs). Each group will have a 4 year follow-up period.

The final analysis will be undertaken shortly after seven years. The primary hypothesis for the study is whether 13-cRA lowered the rate of second primary tumors (SPT). All patients randomized will be grouped according to the assigned treatment. Patients who are either purely lost to follow up or died without a SPT occurring will be included in the actuarial analysis with a censored status on the last day of contact. The primary hypothesis of treatment benefit will be tested using the proportional hazards model.

**Progress:** This protocol closed to patient entry in April 1997, with eight patients enrolled who remain disease free and continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 93166	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9303: Phase III Study of Radiation Therapy, Levamisole, and 5-Fluorouracil versus 5-Fluorouracil and Levamisole in Selected Patients With Completely Resected Colon Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 11/5/1993 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/14/2006

**Study Objective:** To determine whether 5-FU, levamisole and radiation therapy results in superior overall survival when compared to 5-FU and levamisole without radiation therapy in the management of patients with completely resected pathologic stage T4BN0-2 colon cancer and selected patients with T3N1-2 colon cancer.

**Technical Approach:** This randomization clinical trial will compare radiation therapy, 5FU and levamisole with 5FU and levamisole in patients with completely resected colon cancer at high risk for local-regional recurrence and limited risk for system disease.

We will compare 5FU and levamisole, as delivered in the prior intergroup study, with one month of 5FU and levamisole followed by 5-5 1/2 weeks of 5FU, levamisole, and local-regional RT (45-50.4 Gy in 25-28 fractions), followed by 43 weeks of 5FU and levamisole.

**Progress:** This protocol closed to patient entry in December 1996, with one patient enrolled during FY95, who remains disease free and continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 94170	<b>Status:</b> Terminated
<b>Title:</b> SWOG 9313: Phase III Comparison of Adjuvant Chemotherapy With High-Dose Cyclophosphamide + Doxorubicin vs Sequential Doxorubicin Followed by Cyclophosphamide in High-Risk Breast Cancer Patients with 0-3 Positive Nodes		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 9/21/1994 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/14/2006
<b>Study Objective:</b> 1) To compare disease-free survival, overall survival, and toxicity of high-risk primary breast cancer patients with negative axillary lymph nodes or with one to three positive nodes treated with adjuvant high-dose chemotherapy with doxorubicin plus cyclophosphamide, versus high-dose sequential chemotherapy with doxorubicin followed by cyclophosphamide. 2) To obtain tumor tissue for biologic studies.		
<b>Technical Approach:</b> Women with primary breast invasive adenocarcinoma, will be randomized to one of two treatments: 1) High dose doxorubicin + cyclophosphamide x 6 cycles, or 2) High dose sequential doxorubicin x 4 cycles, followed by high dose cyclophosphamide x 3. Women who are postmenopausal and have receptor + will receive Tamoxifen for 5 years.		
<b>Progress:</b> This protocol closed to patient entry in May 1997, with one patient enrolled who remains disease free and continued to be followed at MAMC. The protocol was terminated during FY06, and the surviving patient will continue to be followed under MAMC #99019, SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 95003	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9401: A Controlled Phase III Evaluation of 5-FU Combined with Levamisole and Leucovorin as Surgical Adjuvant Treatment Following Total Gross Resection of Metastatic Colorectal Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 11/18/1994 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10/10/2006

**Study Objective:** To determine in patients who have undergone complete gross surgical resection of metastatic colorectal cancer whether postoperative adjuvant chemotherapy with a new regimen of 5-fluorouracil (5-FU) plus leucovorin plus levamisole will result in improved survival compared to postoperative adjuvant chemotherapy with a standard 5-FU plus levamisole regimen.

**Technical Approach:** Patients will be randomly selected to treatment Arm I or treatment Arm II. Arm I consists of the standard regimen of 5-FU given by rapid intravenous infusion for 5 consecutive days, plus levamisole given by mouth three times daily for three consecutive days every other week for one year. Arm II is a new chemotherapy regimen which adds leucovorin in addition to the 5-FU and levamisole. 5-FU and leucovorin are given by rapid intravenous injection for five consecutive days every four to five weeks for one year. Levamisole is given by mouth three times per day for three days in a row every two weeks during the first two months, then every 2-3 weeks for a total of one year.

**Progress:** This protocol closed to patient entry in September 1996, with one patient enrolled who remains disease free and continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 95093	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9402: Phase III Intergroup Randomized Comparison of Radiation Alone vs Pre-Radiation Chemotherapy for Pure and Mixed Anaplastic Oligodendrogliomas		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 5/19/1995 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2/8/2006
<p><b>Study Objective:</b> 1) overall survival 2) compare time to tumor progression between the two arms 3) the frequency of severe (= grade 3) toxicities will be examined. 4) compare quality of life and neurologic function between the two arms. 5) identify the key histopathologic criteria necessary to make the diagnosis of anaplastic oligodendroglioma and mix oligo-astrocytoma; evaluate the diagnostic and prognostic relevance of chromosomal alterations; evaluate the diagnostic and prognostic relevance of DNA ploidy and indices of proliferation including percent S and percent G2M; study the diagnostic and prognostic relevance of immunohistochemical markers of cellular function and/or glial development; and evaluate the transnational relevance of tumor suppressor genes and oncogenes.</p> <p><b>Technical Approach:</b> This is a non-blinded randomized intergroup study and is different from other randomized trials for malignant glioma in three respects. First, it will evaluate the role of adjuvant chemotherapy in a recognizable subset of patients with malignant glioma, those with oligodendroglial differentiation. Second, the RT treatment volume will be based on a postoperative pre-randomization MR image, rather than the customary preoperative diagnostic CT or MR. Third, in the experimental arm of this study, chemotherapy will be given prior to RT. Patients whose tumors progress on chemotherapy will proceed to RT immediately. There will be a central pathology review prior to randomization, central radiology review to assess response to PCV and to substantiate tumor progression, and a quality of life assessment (QLA) to document the acute and chronic toxicities of chemotherapy and radiation including effects on cognitive function. Surgery and radiotherapy ± PCV may adversely affect a patient's physical and emotional functioning. The Karnofsky performance status (KPS) will measure physical well-being. To complement KPS, the Mini-Mental Status exam (MMSE) will be administered to patients to assess cognitive ability. Assessment of differences in quantitative survival will be performed between the two therapeutic regimens supplemented with qualitative survival by the assessment of KPS, MMSE, and QLA.</p> <p><b>Progress:</b> This protocol closed to patient entry in March 2002, with one patient enrolled who remains disease free and continued to be followed during FY06.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 94163	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9410 (INT 0148): Doxorubicin Dose Escalation, With or Without Taxol, As Part of the CA Adjuvant Chemotherapy Regimen for Node Positive Breast Cancer: A Phase III Intergroup Study		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 1/20/1995 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** To determine (1) whether dose escalation of doxorubicin used as an adjuvant with cyclophosphamide in patients with early breast cancer will increase disease free and overall survival; (2) whether the use of Taxol as a single agent after the completion of 4 cycles of cyclophosphamide and doxorubicin in combination will further improve disease-free and overall survival compared to cyclophosphamide and doxorubicin alone; (3) if Taxol following standard dose cyclophosphamide and doxorubicin will be as effective or more effective than high dose cyclophosphamide and doxorubicin without Taxol; (4) to access the toxicity of the different doses of cyclophosphamide and doxorubicin with and without Taxol using the end point of life threatening or lethal toxicity; (5) whether the longer duration of chemotherapy treatment for patients randomized to receive Taxol is associated with a reduction in local recurrence in patients with lumpectomy and radiotherapy.

**Technical Approach:** Women with breast cancer, who have been treated with either mastectomy or segmentectomy will receive adjuvant chemotherapy. All patients will receive 4 courses of cyclophosphamide and doxorubicin (21 day cycle), but the doxorubicin dose will vary depending upon the randomization. Patients randomized to high dose doxorubicin will also receive G-CSF & ciprofloxacin. Some women will be randomized to receive Taxol after 4 cycles of AC chemotherapy is completed. They will receive taxol day 1 of a 21 day cycle for 4 cycles. Women with ER positive tumors will be given tamoxifen for 5 years.

**Progress:** This protocol closed to patient entry in April 1997, with nine patients enrolled. Four patients died due to disease progression and four patients remain disease free and continued to be followed during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 96095	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9514: Phase III Double-Blind, Placebo-Controlled, Prospective Randomized Comparison of Adjuvant Therapy with Tamoxifen vs. Tamoxifen & Fenretinide in Postmenopausal Women with Involved Axillary Lymph Nodes and Positive Receptors, Intergroup		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 6/21/1996 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 3/15/2006

**Study Objective:** 1) To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen or progesterone receptors who are treated with standard adjuvant tamoxifen vs. tamoxifen and fenretinide; 2) to gain wider experience and toxicity information on the combination of tamoxifen and fenretinide; and 3) to obtain tumor tissue from these patients for future biologic studies of relevance to this patient population.

**Technical Approach:** The present standard of therapy for node positive and ER positive post menopausal women is Tamoxifen alone. There are some studies that suggest that the addition of adjuvant chemotherapy combined with hormonal therapy will prolong relapse free and overall survival. However, not all patients, especially in the over 65 year old age group, can tolerate or want the significant side effects of chemotherapy. Thus, a less toxic regimen is needed. This study attempts to use a chemoprophylactic approach along with the standard Tamoxifen treatment for this group of patients. This new retinoid has shown some effectiveness in Phase I and II studies when given in combination with Tamoxifen to untreated metastatic breast cancer patients. This study will test its use in a Phase III randomized, prospective, placebo-controlled trial. The side effects seem to be fairly minimal except for night blindness which will be closely monitored during this trial.

**Progress:** This protocol closed to patient entry in November 1999, with four patients enrolled who remain disease free and continue to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 96118	<b>Status:</b> Ongoing
<b>Title:</b> SWOG 9515: Phase III Intergroup Trial of Surgery Followed by (1) Radiotherapy vs. (2) Radiochemotherapy for Resectable High Risk Squamous Cell Carcinoma of the Head and Neck		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 9/20/1996 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/10/2006

**Study Objective:** 1) To determine the efficacy of concurrent cisplatin and radiotherapy following surgical resection in patients who have advanced squamous cell carcinoma of the head and neck region; 2) to test whether the use of concurrent chemoradiotherapy following surgery increases locoregional control rates; 3) to determine if the patterns of first failure are changed by the use of concurrent chemotherapy; 4) to determine whether the use of concurrent chemoradiotherapy prolongs disease-free survival and/or overall survival; and 5) to compare the toxicity of concurrent chemoradiotherapy versus radiation alone in the postoperative setting.

**Technical Approach:** In head and neck squamous cell carcinomas with high risk features, there is a 20 to 50 percent recurrence rate after surgical resection. These high risk features include greater than 2 lymph nodes positive, extracapsular extension of cancer in lymph nodes, and positive resection margins. In the past, patients with these high risk features had received radiation therapy for local control. There is evidence, however, that the addition of cisplatin with concurrent radiation therapy may help in local control. This data comes from in vitro as well as in vivo data showing cisplatin may be a radiation sensitizer that may have synergistic local effects on malignancies. The study is a Phase III randomized study that will compare standard radiation therapy against concurrent cisplatin and radiation therapy for resected squamous cell carcinoma of the head and neck. The added toxicities of neuropathy, nausea and emesis, renal failure, and bone marrow suppression are tolerable and can be prevented with medical measures. It is hoped that local recurrence will be reduced with this approach with minimal added toxicity.

**Progress:** This protocol closed to patient entry in May 2000, with one patient enrolled who remains disease free and continued to be followed at MAMC during FY06.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 98112	<b>Status:</b> Ongoing
<b>Title:</b> SWOG C9581: Phase III Randomized Study of Adjuvant Immunotherapy with Monoclonal Antibody 17-1A Versus No Adjuvant Therapy Following Resection for Stage II (Modified Astler-Coller B2) Adenocarcinoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10/20/1998 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/14/2006
<p><b>Study Objective:</b> (1) To determine whether adjuvant treatment with MoAb 17-1A will improve the probability of overall and disease-free survival, and increase disease-free intervals in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer, (2) to evaluate a panel of prognostic markers, in order to correlate these measures with survival and recurrence after adjuvant therapy in patients who have undergone resection of a Stage II (pT3NO or pT4bNO) colon cancer. The specific aims of the companion study will be: (a) to determine whether alterations in the expression of cell cycle related genes (thymidylate synthase, p53, and the cyclin-dependent kinase inhibitors p21 and p27) predict the risk of survival and recurrence in this patient population, (b) to determine whether alterations in markers of metastatic potential-expression of DCC and measures of tumor angiogenesis (microvascular density and vascular endothelial growth factor expression)-predict the risk of survival and recurrence in this patient population, (c) to determine whether a marker of cellular differentiation-sucrase isomaltase-predicts the risk of survival and recurrence in this patient population, and (d) to determine whether interactions among these tumor markers identify subsets of patients with significantly altered outcome.</p> <p><b>Technical Approach:</b> Subjects will be randomized and assigned to one of two treatment groups following standard surgical removal of their tumor. Group 1 will receive standard care which is surgery with no additional therapy after the tumor has been removed. Subjects will continue with routine check-ups, doctor visits and test. Group 2 will receive five antibody treatments using MoAb 17-1A. Subjects will receive the drug by as an intravenous infusion over a 2-hour time period once each 28 days. This 2-hour infusion will be repeated every 4 weeks for a total of 5 treatments. During treatment, various blood tests and x-rays will be used to determine whether the disease has returned. With subject's approval, tissue, body fluids, and other specimens obtained during the normal course of treatment will be forwarded to a special research laboratory for storage and scientific testing. Subjects will also be asked to complete a background information form to help define groups of patient being treated.</p> <p><b>Progress:</b> This protocol closed to patient entry in May 2002, with one patient enrolled in FY98 who continued to be followed at MAMC during FY06.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 99014	<b>Status:</b> Ongoing
<b>Title:</b> SWOG C9741: A Randomized Phase III Trial of Sequential Chemotherapy Using Doxorubicin, Paclitaxel, and Cyclophosphamide, or Concurrent Doxorubicin and Cyclophosphamide Followed by Paclitaxel at 14 or 21 Day Intervals in Women with Node Positive Stage II/IIIA Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 1/26/1999 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 11/21/2006

**Study Objective:** (1) To compare sequential chemotherapy with Doxorubicin, Paclitaxel, and Cyclophosphamide to combined Doxorubicin and Cyclophosphamide followed by Paclitaxel for disease-free and overall survival, (2) to determine whether increasing the dose density of adjuvant chemotherapy (decreasing the interval between chemotherapy courses from 21 to 14 days) will improve disease-free and overall survival, and (3) to compare the toxicity for patients treated with sequential Doxorubicin, Paclitaxel, and Cyclophosphamide with toxicity for patients with concurrent Doxorubicin plus Cyclophosphamide followed by Paclitaxel at 14 and 21 day intervals.

**Technical Approach:** This is a randomized comparison of several aggressive combination chemotherapy regimens in the treatment of high-risk breast cancer due to positive lymph nodes. It compares the current standard of care for node positive breast cancer with several more aggressive variations. All patients will receive the same number of drugs and the same amount of drugs, but the order in which the drugs are given and the time between treatments (2 weeks versus 3 weeks) will be different. Arm 1, patients will receive Doxorubicin once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses followed by Cyclophosphamide once every 3 weeks x 4 total doses. Arm 2, patient will receive Doxorubicin once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses followed by Cyclophosphamide once every 2 weeks x 4 total doses. Arm 3, patients will receive Doxorubicin and Cyclophosphamide once every 3 weeks x 4 total doses followed by Paclitaxel once every 3 weeks x 4 total doses. Arm 4, patients will receive patients will receive Doxorubicin and Cyclophosphamide once every 2 weeks x 4 total doses followed by Paclitaxel once every 2 weeks x 4 total doses. G-CSF and Ciprofloxacin will be given concurrent with each arm to help ameliorate side effects of the treatments.

**Progress:** This protocol closed to patient entry in March 1999, with three patients enrolled. One patient is deceased and two patients remain disease free and continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200036	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E1199: A Phase III Study of Doxorubicin-Cyclophosphamide Therapy Followed by Paclitaxel or Docetaxel Given Weekly or Every 3 Weeks in Patients with Axillary Node-Positive Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 8/29/2000 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/4/2006

**Study Objective:** (1) To determine whether docetaxel improves disease-free survival and overall survival when compared to paclitaxel following 4 cycles of doxorubicin-cyclophosphamide therapy (2) To determine whether weekly administration of taxanes (paclitaxel or docetaxel) for 12 weeks improves disease-free survival and overall survival when compared with the conventional (every 3 weeks) schedule for 4 cycles following 4 cycles of doxorubicin-cyclophosphamide therapy (3) To compare the toxicity of docetaxel given weekly for 12 weeks to that of paclitaxel given every 3 weeks for 4 cycles (4) To compare the toxicity of paclitaxel given weekly for 12 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles (5) To compare the toxicity of paclitaxel given every 3 weeks for 4 cycles to that of docetaxel given every 3 weeks for 4 cycles and (6) To compare the toxicity of paclitaxel given weekly for 12 weeks to that of docetaxel given weekly for 12 weeks.

**Technical Approach:** This study compares aggressive chemotherapy schedules to standard of care for high risk node positive breast cancer. Eligible patients will be randomized into one of four treatment arms: Arm A, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxol (the standard treatment); Arm B, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxol (lower dose than standard); Arm C, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxotere (medium dose); and Arm D, 12 weeks of Adriamycin and Cytoxan followed by 12 weeks of Taxotere (low dose).

All Arms will receive Adriamycin and cyclophosphamide, IV once every 3 weeks for 4 cycles. Then Arm A will receive Taxol, IV once every 3 weeks for 4 treatments. Arm B will receive Taxol IV once a week for 12 weeks of treatment. Arm C will receive Taxotere IV once every 3 weeks for 4 treatments. Arm D will receive Taxotere once a week for 12 weeks of treatment.

**Progress:** This protocol closed to patient entry in January 2002, with fourteen patients enrolled. One patient died and thirteen remain disease free and continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 99071	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E2197: Phase III Study of Adriamycin/Taxotere vs. Adriamycin/Cytosan for the Adjuvant Treatment of Node Positive or High Risk Node Negative Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 7/20/1999 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** To determine whether Adriamycin/Taxotere will improve disease-free survival and overall survival when compared to Adriamycin/Cytosan in lymph node positive (1-3 positive nodes) and high risk lymph node negative breast cancer. To compare toxicity of Adriamycin/Taxotere to Adriamycin/Cytosan.

**Technical Approach:** This is multi-site study with randomization to one of two arms: Adriamycin/Taxotere (AT) or Adriamycin/Cytosan (AC). The dosages for the AT group: Adriamycin 60 mg/M2 IV and Taxotere 60 mg/M2 IV over 1 hour infusion every 3 weeks x 4 cycles. Cipro 500 mg PO b.i.d. starting Day 8 and continuing x 10 days. If a patient is allergic to Cipro, an alternative broad spectrum antibiotic may be used. Decadron 8 mg PO b.i.d., beginning one day prior to treatment with Taxotere and continued for two additional days; repeat q 3 weeks x 4 cycles. The dosages for the AC group: Adriamycin 60 mg/m2 IV and Cytosan 600 mg/ml IV. Every 3 weeks x 4 cycles. In both groups, post-menopausal patients who are ER and/or PR positive will receive Tamoxifen 20 mg PO daily x 5 years at the completion of chemotherapy. G-CSF: Patients who have an episode of febrile neutropenia should be placed on G-CSF according to ASCO Guidelines. Patients who have febrile neutropenia after a subsequent dose of chemotherapy in spite of G-CSF should have the chemotherapy doses lowered by 25%.

**Progress:** This protocol closed to patient entry in January 2000, with two patients enrolled who continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204066	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E2496 Randomized Phase III Trial of ABVD Versus Stanford V +/- Radiation Therapy in Locally Extensive and Advanced Stage Hodgkin's Disease With 0-2 Risk Factors		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC John B. Halligan, MC; LTC William B. Reece, MC		
<b>Start - Completion:</b> 8/17/2004 - Apr 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** (1) To compare the failure-free survival in patients with locally extensive and advanced stage Hodgkin's disease (HD) treated with standard ABVD chemotherapy + radiotherapy versus patients given Stanford V chemotherapy + radiotherapy. (2) To assess overall survival and freedom from progression in these patients at 5 and 10 years. (3) To assess secondary endpoints: pulmonary function, incidence of second cancers, reproductive function (at baseline and at 5 years) and deaths from causes other than Hodgkin's disease.

**Technical Approach:** SWOG E2496 is a national intergroup randomized Phase III trial of two treatment regimens for the treatment of locally extensive and advanced stage Hodgkin's disease. Subjects with bulky disease will receive radiation therapy in addition to chemotherapy in the control ABVD treatment Arm and subjects with lymphoma masses > 5 cm will receive radiation therapy on the Stanford V Arm. The primary endpoint of the trial is failure free survival. Laboratory endpoints include relative risk of death and treatment failure in subjects with EBV-positive disease, the concordance between three different EBV detection techniques, and the relationship of EBV viral DNA clearance for the two treatment arms. Laboratory studies will also investigate the relationship between T-cell response and EBV status and the time course of the T-cell response. This is a national intergroup study expected to accrue 204 subjects per year for a total of 850 subjects. At MAMC 2 subjects per year are expected to enroll. Data and statistical analysis will be conducted by the sponsoring study group, ECOG (Eastern Cooperative Oncology Group) with planned interim analyses at 33% and 67% of the number of anticipated treatment failures. It is expected that 3 years of follow-up will be required after complete accrual.

**Progress:** This protocol closed to enrollment in April 2006; four patients enrolled at MAMC. Three patients remain in follow-up and one transferred to another facility.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200040	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E4494: Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 1/25/2000 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/4/2006

**Study Objective:** (1) To compare CHOP treatment with or without chimeric anti-CD20 monoclonal antibody (IDEC-C2B8) in elderly patients with diffuse mixed, diffuse large cell, and immunoblastic large cell non-Hodgkin's lymphoma of B lineage with respect to response rate, the time to treatment failure, toxicity and survival, (2) To compare IDEC-C2B8 monoclonal antibody as maintenance therapy to observation alone after CHOP chemotherapy with respect to time to treatment failure, duration of response, toxicity and survival after an initial response to induction therapy of CHOP + IDEC-C2B8, and (3) To determine if maintenance therapy with IDEC-C2B8 results in the conversion of any partial responses to a complete response.

**Technical Approach:** This study adds a new drug, chimeric anti-CD20 monoclonal antibody, to the standard treatment (cyclophosphamide, doxorubicin, vincristine and prednisone, CHOP) of Non-Hodgkin's Lymphoma. Patients eligible for this study will be randomized to receive or not to receive IDEC-C2B8 (anti-CD20) in conjunction with chemotherapy. Treatment Arm A, CHOP plus Anti-CD20 will receive the study drug IV over 6 to 12 hours on Days 7 and 3 before the first treatment cycle of CHOP. Anti-CD20 will also be given 48 hours prior to cycles 3, 5 and 7 of CHOP. Treatment Arm B will receive CHOP for a minimum of 6 or a maximum of 8 cycles. Restaging of disease after 4 cycles and again after 6 cycles will be done to determine response and eligibility to be randomized to Maintenance Treatment Arms C & D. Arm C will continue to receive Anti-CD20 IV, four weekly doses every 6 months for 2 years. Arm D will be the observation group.

**Progress:** This protocol closed to patient entry in May 2001, with two patients enrolled. One patient died and the other patient continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202010	<b>Status:</b> Ongoing
<b>Title:</b> SWOG E5597: Phase III Chemoprevention Trial of Selenium Supplementation in Persons with Resected Stage I Non-Small Cell Lung Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10/23/2001 - Oct 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/22/2006

**Study Objective:** (1) To evaluate the efficacy of selenium supplementation in reducing the incidence of second primary lung tumors in patients who have been treated for Stage I non-small cell cancer with complete surgical resection, (2) to evaluate the qualitative and quantitative toxicity of a selenium supplementation in a daily administration schedule and (3) to compare the incidence of specific cancers and mortality from cancer as well as overall survival of patients treated with selenium supplementation versus patients treated with placebo.

**Technical Approach:** Selenium chemo-prevention may improve upon patients with high risk of second lung primaries as well other aero digestive tract tumors.

**Progress:** This protocol remains open to patient entry, with two patients enrolled at MAMC. Both patients remain on active study treatment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202012	<b>Status:</b> Ongoing
<b>Title:</b> SWOG GO182: A Phase III Randomized Trial of Paclitaxel and Carboplatin Versus Triplet or Sequential Doublet Combinations in Patients with Epithelial Ovarian or Primary Peritoneal Carcinoma		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Jane Shen-Gunther, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10/23/2001 - Nov 2004	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 9/29/2006

**Study Objective:** (1) To compare the efficacy of each experimental arm with the control arm (paclitaxel and Carboplatin). Efficacy will be determined through analysis of overall survival and progression-free survival, (2) To compare the response rate in patients with measurable disease, toxicities and complications of each treatment regimen and to describe dose-intensity and cumulative dose delivery for each regimen and (3) To extend the accrual into a study initiated with GOG Protocol #0172 which will assess whether inactivated BRCA1 and /or BRCA2 is a prognostic factor for clinical outcome.

**Technical Approach:** This study is designed to compare the effectiveness and side effects of several chemotherapy combinations (Paclitaxel, Carboplatin, Gemcitabine, Topotecan, Doxil [Liposomal Doxorubicin]) which are known to be effective in women with ovarian or primary peritoneal cancer. This study will enroll adult females with histologic diagnosis of primary peritoneal carcinoma or epithelial ovarian carcinoma, Stage III or IV, with either optimal or suboptimal residual disease following initial surgery.

**Progress:** This study closed to patient entry in September 2004, with eight patients enrolled. Three patients continued to be followed at MAMC during FY06.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 97070	<b>Status:</b> Ongoing
<b>Title:</b> SWOG JBR.10 (NCIC CTG BR.10): A Phase III Prospective Randomized Study of Adjuvant Chemotherapy with Vinorelbine and Cisplatin in Completely Resected Non-small Cell Lung Cancer with Companion Tumour		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 3/21/1997 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2/22/2006
<b>Study Objective:</b> 1) To compare the duration of overall survival (OS) between completely rejected patients with T2 NO, T1-2N1 non-small cell lung cancer (NSCLC) who have received either adjuvant chemotherapy with vinorelbine and cisplatin or observation alone. 2) To determine disease-free survival. 3) To confirm the prognostic significance of ras mutations when present in the primary tumor. 4) To provide a comprehensive tumor bank linked to a clinical data base for the further study of molecular markers in rejected NSCLC. 5) To measure and compare health related quality of life in both treatment arms throughout the study period. 6) To evaluate toxicity related to chemotherapy.		
<b>Technical Approach:</b> The role of adjuvant chemotherapy in Non-small cell lung cancer is controversial. Most clinical trials have shown no benefit to adjuvant chemotherapy. In the early 80's the lung cancer study group showed some benefit with combination chemotherapy in terms of survival, however, the control arm was not a strict observational arm and contained a "biological response modifier" in it. Thus with recent improved survival in Stage IV lung cancer shown compared to observation, it is assumed that using platinum based therapies may enhance survival in patients that have completely rejected non-small cell lung cancer. In patients with rejected Stage I, II, and III Non-small cell lung cancer it is known that the long term survival rates are 50 to 60%, 30 to 50%, and 19 to 49% respectively. It is thus the aim of this study to assess whether adjuvant therapy with Cisplatin and Vinorelbine will improve survival and relapse free survival compared to observation. In addition to the above study, tissue samples will be sent to the University of Washington for evaluation of Ras mutations to assess its prognostic importance.		
<b>Progress:</b> This protocol closed to patient entry in April 2001, with two patients enrolled who remain disease free and continued to be followed at MAMC during FY06.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 99040	<b>Status:</b> Ongoing
<b>Title:</b> SWOG JMA.17: A Phase III Randomized Double-Blinded Study of Letrozole Versus Placebo in Women with Primary Breast Cancer Completing Five or More Years of Adjuvant Tamoxifen		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 2/23/1999 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** Primary: To determine the disease-free survival and overall survival (all cause mortality) for women who have previously received  $\geq 5$  years of adjuvant Tamoxifen, randomized to receive wither Letrozole 2.5 mg daily or placebo daily for 5 years.

Secondary: To evaluate the incidence of contralateral breast cancer. To evaluate the long term clinical and laboratory safety of Letrozole with special attention to: lipid profile as assessed by blood sampling (in a limited number of centers), cardiovascular morbidity and mortality (i.e. significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty or coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) as assessed by reported toxicity, the incidence of all bone fractures (with particular emphasis on hip and wrist fractures as indicators of osteoporosis) as assessed by reported toxicity, changes in bone density (in a limited number of centers), common toxicities as assessed by reported toxicity.

Third: To evaluate overall quality of life.

**Technical Approach:** This is a multi-centre, double-blind, placebo-controlled parallel randomized trial of the NCIC Clinical Trials Group, supported by Novartis. Patients will be stratified by: receptor status at diagnosis (positive, unknown), lymph node status at diagnosis (negative, positive, unknown), and a prior adjuvant chemotherapy (yes, no). Patients will be centrally randomized to receive one of the following treatments: Arm 1 (letrozole): 2.5 mg po daily x 5 years or Arm 2 (Placebo): po daily x 5 years.

**Progress:** This protocol closed to patient entry in December 2005, with thirteen patients enrolled; two patients continue on Letrozole. One patient is deceased; twelve patients continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200120	<b>Status:</b> Ongoing
<b>Title:</b> SWOG N9831: Phase III Trial of Doxorubicin and Cyclophosphamide (AC) Followed by Weekly Paclitaxel With or Without Trastuzumab as Adjuvant Treatment for Women with HER-2 Over-expressing or Amplified Node Positive or High-Risk Node Negative Breast Cancer (an Intergroup Study)		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 8/22/2000 - Dec 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 7/18/2006

**Study Objective:** (1) To compare the combination AC followed by weekly paclitaxel with the sequential schedule of the combination of AC, weekly paclitaxel, and trastuzumab in terms of disease-free survival (DFS). (2) To compare the combination of AC followed by weekly paclitaxel with the combination of AC followed by the combination of weekly paclitaxel and trastuzumab in terms of DFS. (3) To compare the sequential schedule of AC, weekly paclitaxel, and trastuzumab with the combination of weekly paclitaxel and trastuzumab in terms of DFS. (4) To compare the cardiotoxicities of (a) AC followed by weekly paclitaxel, (b) AC followed by weekly paclitaxel followed by weekly trastuzumab, and (c) AC followed by weekly paclitaxel and trastuzumab followed by weekly trastuzumab.

**Technical Approach:** Subjects will be randomly assigned to one of three arms: Arm A - Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), Taxol by vein over 1 hour one day every week for a total of 12 treatments. Total length of treatment will be about six months. Arm B - Subjects will be given Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), you will get Taxol by vein over 1 hour one day every week for a total of 12 treatments. After all treatment with Taxol is done (about week 24), Herceptin by vein one day every week for one year. The first dose of Herceptin will be given over about 90 minutes. Subjects will be watched for 1 hour after the first dose of Herceptin. If they do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about 18 months. Arm C - Subjects will be given Adriamycin and Cytosan (AC) by vein over about 30 minutes one day every three weeks for a total of four treatments. After all treatment with AC is done (about week 12), subjects will be given Taxol, by vein over 1 hour, plus Herceptin, by vein one day every week, for a total of 12 treatments. After all treatment with Taxol plus Herceptin is done (about week 23), subjects will get Herceptin alone one day every week for six months. The first dose of Herceptin will be given over about 90 minutes. You will be watched for 1 hour after the first dose of Herceptin. If subjects do well this first dose, other doses will be given over about 30 minutes. Total length of treatment will be about one year.

Regardless of which treatment, at the end of all chemotherapy, subject may also get Tamoxifen, if estrogen or progesterone receptor positive, for five years. If subjects had a lumpectomy, they will also get radiation therapy after chemotherapy has ended. Blood samples will be taken before the start treatment for research use. Subjects will be followed indefinitely.

**Progress:** This protocol closed to patient entry in April 2005, with nine patients enrolled. One patient's death was unrelated to study participation, two patients removed from the study due to

decreases in LVF, and the remaining six patients completed study treatment. Eight patients continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201136	<b>Status:</b> Completed
<b>Title:</b> SWOG S0009: A Phase II Evaluation of Neoadjuvant Chemotherapy, Interval Debulking Followed by Intraperitoneal Chemotherapy in Women with Stage III and IV Epithelial Ovarian Cancer, Fallopian Tube Cancer or Primary Peritoneal Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC; LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 9/25/2001 - Aug 2004	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/24/2005
<b>Study Objective:</b> (1) To evaluate the overall survival and progression-free survival in Stage III or IV epithelial ovarian, fallopian tube or primary peritoneal carcinoma patients with bulky disease and/or malignant pleural effusions treated with neoadjuvant intravenous paclitaxel and Carboplatin, cytoreductive surgery and intravenous/intraperitoneal paclitaxel and intraperitoneal Carboplatin, (2) To estimate the percent of patients successfully cytoreduced to optimal disease (<1 cm residual) following neoadjuvant chemotherapy, (3) To evaluate the toxicities associated with this therapy, and (4) To explore the relationship between tumor p53 expression, cellular proliferation rate as measured by PCNA and apoptotic rate, and human tumor cloning assay results at time of debulking surgery with progression-free survival and overall survival in patients undergoing cytoreductive surgery.		
<b>Technical Approach:</b> This protocol evaluates the effectiveness and side effects of a treatment regimen for advanced ovarian, peritoneal, and fallopian tube cancers. The treatment consists of intravenous chemotherapy of paclitaxel and carboplatin (3 treatments), followed by surgery, followed by a combination of intravenous paclitaxel and intra-peritoneal carboplatin and paclitaxel (6 treatments).		
<b>Progress:</b> This protocol closed enrollment in February 2006, when accrual goals were met. No subjects enrolled at MAMC.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201137	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0012: A Comparative Randomized Study of Standard Doxorubicin and Cyclophosphamide Followed by Weekly Paclitaxel Vs. Weekly Doxorubicin and Daily Oral Cyclophosphamide Plus G-CSF Followed by Weekly Paclitaxel as Neoadjuvant Therapy for Inflammatory and Locally Advanced Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 9/25/2001 - Oct 2004	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** (1) To compare the microscopic pathologic response rates in patients with inflammatory and estrogen-receptor negative locally advanced breast cancer treated with weekly Doxorubicin and daily oral Cyclophosphamide given with G-CSF support to in-patients treated without "standard" Doxorubicin and Cyclophosphamide regimen given every three weeks, (2) To compare the toxicities of these two regimens, (3) To compare the delivered dose intensity of these two regimens, and (4) To assess the association between microscopic pathologic complete response and clinical complete response at the primary tumor site in these patients.

**Technical Approach:** This trial is designed to compare two different treatment regimens for breast cancer prior to surgery to see if one works better against breast cancer than the other in very poor risk patients who may benefit from up-front chemotherapy. The standard regimen of Adriamycin and Cyclophosphamide given Day 1 every 21 days is compared to a regimen of Adriamycin given once a week for 15 weeks and oral Cyclophosphamide daily for 15 weeks. Filgrastim and trimethoprim sulfa will also be given in this regimen to protect against toxicity of the chemotherapy agents used.

**Progress:** This protocol remains open to patient entry, with three patients enrolled. One patient is deceased and two continued to be followed at MAMC in FY06. No internal adverse events were reported and no patients received study treatment in the past year.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203084	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0016, A Phase III Trial of CHOP + Rituximab vs. CHOP + Iodine-131-Labeled Monoclonal Anti-B1 Antibody (Tositumomab) for Treatment of Newly Diagnosed Follicular Non-Hodgkin's Lymphomas		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10/29/2003 - Jul 2006	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** (1) To compare progression-free and overall survival between CHOP-Rituximab vs. CHOPP+I-131 tositumomab. (2) To compare the response rate between CHOP-Rituximab vs. CHOPP+I-131. (3) To compare the toxicities of these two regimens. Also, to compare the molecular remission rates by measuring colonel rearrangements in the bone marrow at baseline and at one year post-treatment.

**Technical Approach:** This is a national trial with a goal accrual of 500 patients to determine if a radioisotope labeled Anti-CD20 antibody (tositumomab) added to standard CHOP chemotherapy is superior to a combination of CHOP plus the uncongealed anti-CD20 antibody Rituximab. Specifically the endpoints will include disease free survival, overall survival, response rate, rate of molecular remission and data will also be collected on the toxicity of therapy. Data analysis will be analyzed by the SWOG Data and Safety Monitoring Committee (DSMC). The power analysis by the SWOG DSMC includes a sample size of 250 per treatment arm will detect a response rate difference of 6% between treatments. Eligible subjects will be randomized into one of the two study arms. (1) CHOP chemotherapy plus the rituximab antibody, 6, 21 day treatment cycles or (2) CHOP chemotherapy followed by the I-131 anti-B1 antibody, tositumomab, 6, 21 day treatment cycles. Four to six weeks after completion of chemotherapy, subjects will receive treatment with by the I-131 anti-B1 antibody, tositumomab. Also, at the time of surgery, tumor tissue, tumor fluid, and blood will be collected and used for specific experimental molecular tests, called P53, PCNA, Apoptosis and Human tumor cloning assay.

**Progress:** This protocol is open to enrollment, with three subjects enrolled who completed treatment. One subject is deceased due to progressive disease; two remain in remission and continued on follow-up during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204052	<b>Status:</b> Completed
<b>Title:</b> SWOG S0023, A Phase III Trial of Cisplatin/Etoposide/Radiotherapy with Consolidation Docetaxel Followed by Maintenance Therapy with ZD1839 or Placebo in Patients With Inoperable Locally Advanced Stage III Non-Small Cell Lung Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC John B. Halligan, MC; LTC William B. Reece, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 11/15/2004 - Apr 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 2/28/2006

**Study Objective:** (1) To assess whether maintenance therapy with ZD1839 as compared to placebo following induction cisplatin/etoposide/radiotherapy plus consolidation docetaxel improves overall survival and progression-free survival in patients with unresectable Stage III non-small cell lung cancer (NSCLC). (2) To describe the toxicity profile of long term administration of ZD1839. To obtain samples for correlative studies as outlined in S9925.

**Technical Approach:** This study is an intergroup Phase III randomized, placebo-controlled trial of a standard chemotherapy / radiation therapy regimen for inoperable Stage III NSCLC followed by randomization to maintenance ZD1839 (Iressa) versus placebo for 5 years. This national trial has a goal accrual of 840 over 3.5 years or about 240 patients per year with 3 patients per year at MAMC. The major end-points of the trial are progression-free survival and overall survival. Data analysis will be conducted by the SWOG monitoring committee with a planned interim analysis after 400 patients have been accrued to see if pre-determined criteria for early termination of the study have been met. The trial is powered to detect a 33% increase in median survival of the treatment arm.

**Progress:** This protocol closed to enrollment, with three patients enrolled; all deceased due to progressive disease. A closure letter will be submitted to permanently close study site.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204123	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0106, A Phase III Study of the Addition of Gemtuzumab Ozogamicin (Mylotarg®) Induction Therapy Versus Standard Induction With Daunomycin and Cytosine Arabinoside Followed by Consolidation and Subsequent Randomization to Post-Consolidation Therapy With Gemtuzumab Ozogamicin (Mylotarg®) or No Additional Therapy for Patients Under Age 56 With Previously Untreated DeNovo Acute Myeloid Leukemia (AML)		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 3/21/2005 - Jan 2012	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 9/29/2006

**Study Objective:** (1) To compare disease-free survival (DS) of patients under age 56 with previously untreated, de novo, non-M3, MAL who received gemtuzumab ozogamicin as post-consolidation therapy versus patients who received no post-consolidation therapy. (2) To compare the complete remission (CR) rate achieved by the addition of gemtuzumab ozogamicin to standard induction chemotherapy to that achieved with standard induction chemotherapy in patients under the age of 56 with previously untreated, de novo, non-M-3 AML. The durability of complete response will also be measured. (3) To estimate the frequency and severity of toxicities of the addition of gemtuzumab ozogamicin to induction therapy and post consolidation therapy. (4) To evaluate the prognostic significance of CD33 expression on the response rate of those patients who receive gemtuzumab ozogamicin. (5) To evaluate the prognostic significance of FLT3 mutations prior to therapy, and of minimal residual disease in remission specimens collected before and after consolidation therapy and after post-consolidation therapy with gemtuzumab ozogamicin. (6) To evaluate the prognostic significance of the flow cytometric detection of minimal residual disease in specimens collected before and after consolidation therapy and after post-consolidation therapy with gemtuzumab ozogamicin.

**Technical Approach:** This is a randomized phase III trial comparing standard induction chemotherapy for AML with or without the anti-leukemia monoclonal antibody Gemtuzumab ozogamicin (Mylotarg®). Patients will be further randomized for post-consolidation treatment with Gemtuzumab ozogamicin (Mylotarg®) versus no post-consolidation treatment. Due to enhanced toxicity in older patients, this trial is limited to adult patients less than age 56 at the time of study entry. The end points of the trial are to compare disease free survival, complete remission rates and to determine toxicities of each treatment Arm. The trial will also investigate the prognostic significance of CD33 expression, FLT-3 mutations, and the flow cytometric detection of minimal residual disease. The goal accrual of this trial is 684 patients over 5 years with an expected enrollment of 2 patients per year at MAMC.

**Progress:** This protocol remains open to enrollment with no patients enrolled during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204034	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0221, Phase III Trial of Continuous Schedule AC + G Vs. Q 2 Week Schedule AC, Followed by Paclitaxel Given Either Every 2 Weeks or Weekly for 12 Weeks as Post-Operative Adjuvant Therapy in Node-Positive or High-Risk Node-Negative Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 2/26/2004 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** (1) To compare the disease-free survival of patients with node-positive or high-risk node-negative breast cancer treated with the combination of doxorubicin and cyclophosphamide given every 2 weeks with Pegfilgrastim support with that of patients treated with weekly doxorubicin and daily oral cyclophosphamide with filgrastim support, with both treatments to be followed by paclitaxel given according to one of two schedules. (2) To compare the disease-free survival of patients with node-positive or high-risk node-negative breast cancer treated with either 12 weeks of weekly paclitaxel or paclitaxel given every 2 weeks with Pegfilgrastim support for 6 cycles following treatment with one of the two doxorubicin/cyclophosphamide regimens discussed above. (3) To compare the overall survival produced by the four treatment arms. (4) To compare the toxicity of the four treatment arms. (5) To examine the association of putative prognostic markers with outcome and the interaction of these markers with treatment.

**Technical Approach:** This is a 4-arm phase III randomized trial of two different dose-dense doxorubicin plus cyclophosphamide chemotherapy regimens followed by two different schedules of taxol administration used for the treatment of node positive and high risk node negative breast cancer. Major endpoints of the trial are disease free survival and overall survival with an anticipated accrual of 2000 patients per year for a goal of 4500 patients accrued over 2.2 years. The study DSMC will perform an interim analysis at years 2.5, 4 and 6.

**Progress:** This protocol is open to enrollment with 16 patients enrolled. One patient is deceased and the others remain on treatment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204094	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0226, Phase III Randomized Trial of Anastrozole Versus Anastrozole and Fulvestrant as First Line Therapy for Post Menopausal Women With Metastatic Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 9/29/2004 - Jun 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 6/6/2006

**Study Objective:** (1) To compare time to tumor progression in post-menopausal women with metastatic breast cancer treated with Anastrozole versus Anastrozole and Fulvestrant. (2) To compare clinical benefit (CR, PR, confirmed or unconfirmed, or stable disease >24 weeks) and overall survival for this cohort of patients. (3) To assess the adverse events of Anastrozole as compared to Anastrozole and Fulvestrant in this cohort of patients. (4) To assess the prognostic significance of subtypes of ER positive and HER-2 status. (5) To assess parameters of estrogen and clinical pharmacology and estrogen levels as outlined in Sec. 15.4. (6) To compare the Anastrozole plasma levels on each treatment arm at 8 weeks, 16 weeks and 24 weeks after randomization.

**Technical Approach:** S0226 is a randomized Phase III trial of Anastrozole versus Anastrozole plus Fulvestrant as first line endocrine therapy for metastatic breast cancer. The end-points of the trial are to assess the time to tumor progression of each of these treatments, to assess response rates and to assess overall survival of patients. The trial will also assess the adverse effects of each treatment arm and the prognostic significance of tumor ER status and HER2 status. Pharmacokinetic data on Anastrozole plasma levels and serum estradiol levels will be measured in both treatment groups. The trial has a national goal accrual of 230 patients per year for 3 years, with a goal accrual of 5 patients per year here at Madigan. All data evaluation will be done through the SWOG. There will be a planned interim analysis of progression free survival after 50% and 75% of national goal accrual.

Patients will be randomized to receive either 1 mg Anastrozole by mouth every day or 1 mg Anastrozole orally every day and 250 mg of Fulvestrant intramuscular injection once every 28 days. This schedule will continue until disease worsens or side effects are unacceptable. Fulvestrant may be given if disease worsens and if other treatment is not required right away. The first fifty patients in each group will have blood drawn to measure drug levels.

**Progress:** This protocol remains open to enrollment, with no patients enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204064	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0230, Phase III Trial of LHRH Analog Administration During Chemotherapy to Reduce Ovarian Failure Following Chemotherapy in Early Stage, Hormone- Receptor Negative Breast Cancer		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; LTC David E. McCune, MC; LTC John B. Halligan, MC		
<b>Start - Completion:</b> 7/27/2004 - Apr 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** (1) To compare the rate of premature ovarian failure at two years following standard adjuvant chemotherapy with or without the addition of ovarian suppression with a LHRH analog during chemotherapy in premenopausal women with early stage, hormone-receptor negative breast cancer. (2) To compare rates of ovarian dysfunction at one year and two years following standard adjuvant chemotherapy with or without ovarian suppression and to evaluate ovarian reserve in the two groups at one and two years. In addition, this study will describe pregnancy and other fertility information in the two groups after treatment and during the five year follow-up period.

**Technical Approach:** This is a randomized national phase III trial comparing standard adjuvant chemotherapy with chemotherapy plus Goserelin in pre-menopausal women with Stage I, II or IIIA Estrogen receptor negative and progesterone receptor negative breast cancer. Suppression of ovarian function during chemotherapy with a LHRH analog has demonstrated high rates of ovarian preservation in small studies. Outcome variables include the rate of amenorrhea at the completion of chemotherapy, at one year and at two years following treatment. Serum levels of FSH, estradiol and inhibin B will also be obtained at these same time points. Fertility information to include the number of successful pregnancies and the number of miscarriages will be compared at one, two and five years after treatment. National accrual is 416 patients over three years of which an estimated 3 per year will be enrolled at MAMC.

**Progress:** This study remains open to enrollment, with no patients enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206068	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0520: Phase II Study of PXD101 (NSC-726630) in Relapsed and Refractory Aggressive B-Cell Lymphomas		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 7/24/2006 - May 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objectives: (1) To evaluate response rate and toxicity in patients with relapsed and refractory aggressive B-cell lymphoma treated with this regimen. (2) To estimate the 6-month progression-free survival rate in patients with relapsed and refractory aggressive B-cell lymphoma with single agent PXD101 therapy. Correlative study objectives: (1) to assay the MHC Class II proteins (HLA-DR, DP, DQ), TUNEL and CD8 infiltration status by immunohistochemistry on paired pre- and post-treatment tumor samples for 20 patients on the enrolled, (2) to measure CIITA and HLA-DR mRNA expression using quantitative RT-PCR, and to explore in a preliminary manner the associations of these markers and progression-free survival and (3) to evaluate paired pre- and post-treatment peripheral blood mononuclear cells (PBMCs) from patient for histone acetylation conducted on pre- and post-needle core biopsies.

**Technical Approach:** This is a Phase II, open label, multi-site study of PXD101 in relapsed and refractory aggressive B-cell lymphoma. This study will enroll a total of 60 subjects (up to 3 at MAMC) with diffuse large, Burkitt's, Burkitt-like, primary mediastinal lymphoma. Patients will receive PXD101 at a dose of 1,000 mg/m<sup>2</sup>, as a 30 minute IV infusion, on Days 1-5 of a 21 day cycle. Nausea, vomiting, anemia, neutropenia and dehydration will be treated according to institutional standards. Diarrhea will be treated with loperamide. Treatment will be given on Days 1-5 of a 21 Day cycle. Physicals, laboratory tests and adverse event evaluation will be done prior to each subsequent cycle. Disease assessment will be done after Cycle 3, and then every 4 cycles until progression is documented. Patients will be removed from treatment after disease progression, symptomatic deterioration, unacceptable toxicity or completion of 2 years of treatment. Off-treatment evaluation will include monitoring for disease progression and survival for up to a total of 3 years. The primary goal of this study is to assess the response probability in patients with relapsed or refractory aggressive B-cell lymphoma treated with PXD101. Secondary endpoints will include toxicity, overall survival, time to treatment failure and time to progression. It is assumed that this therapy will be of no further interest if the true response probability is 5% or less, and of interest if the true response probability is 20% or more. The study has a two-stage design. If at least one of the first 20 patients responds, an additional 20 patients will be enrolled.

**Progress:** This protocol is open to patient entry, with no patients enrolled during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 91094	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9007 (ECOG S9007), Cytogenetic Studies in Leukemia Patients		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 2/7/1992 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/12/2006

**Study Objective:** (1) To estimate the frequencies and prognostic significance of cytogenetic abnormalities in marrow or blood cells of leukemia patients prior to treatment on Southwest Oncology Group protocols and at various times in the course of their treatment, (2) To estimate correlations between the presence of cytogenetic features and of clinical, pathophysiological, cellular, or molecular characteristics in these patients and (3) To provide quality control for all Southwest Oncology Group cytogenetic data.

**Technical Approach:** This is a companion protocol for all Southwest Oncology Group leukemia protocols. Bone marrow or peripheral blood specimens will be forwarded to a SWOG referral cytogenetics laboratory (Oregon Health Sciences University, Portland, Oregon is the nearest to Madigan Army Medical Center). The referral lab will return a cytogenetics report to MAMC. Specimens will be collected as outlined in each individual leukemia protocol.

**Progress:** This protocol is the cytogenetic companion study to SWOG leukemia treatment protocol S0106. It remains open to enrollment with no subjects enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 99019	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9808: Long-Term Follow-Up Protocol: An Administrative Tool		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 10/20/1998 - Indef	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10/10/2006

**Study Objective:** To relieve the burden on Institutional Review Boards at Southwest Oncology Group Institutions for continuing review of protocols that are closed to patient registration, and on which no patients are currently receiving protocol treatment.

**Technical Approach:** When a study has been closed to patient accrual and patients have finished treatment, it still requires submission of data to the Southwest Oncology Group to report survival and remission status and occurrence of adverse events. On an annual basis, the Southwest Oncology Group Operations Office will notify the institutions as to which protocols are eligible for transfer to the Long Term Follow-Up protocol by periodically revising the list of applicable protocols. The institutional Principal Investigator or IRB will ultimately decide for the local institution whether the protocol should be included in this protocol or continue to be reviewed on its own. A report will be prepared and submitted for annual IRB review at individual institutions. This report will include title and date closed to patient entry.

**Progress:** During FY06, the following protocols continued to have patients followed under this long-term follow-up tool: 8516, 1 patient; 8794, 1 patient; 8809, 2 patients; 9008, 1 patient; 9035, 1 patient; 9133, 2 patients; 9304, 1 patient; and 9349, 2 patients.

Protocols terminated during FY06 and patients added to this administrative tool are: 8814, 3 patients; 8897, 6 patients; and 9313 1 patient.

Protocols that no longer required follow-up data during FY06: 8294, 5 patients; 9003, 1 patient; and 9415, 1 patient.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205035	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9910 Leukemia Centralized Reference Laboratories and Tissue Repositories, Ancillary		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 3/18/2005 - Feb 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/4/2006

**Study Objective:** (1) To develop and apply laboratory assays for the rapid and precise diagnosis of leukemia patients and identify biologic, genetic, and molecular parameters that distinguishes different subtypes of human leukemia with differing responses to therapy. (2) To develop risk-adapted therapeutic approaches in which biologic, genetic, and molecular parameters are used to target individual patients to tailored therapeutic regimens, or, to randomize and stratify patients to different treatment arms of a therapeutic trial. (3) To develop new automated and standardized laboratory methods for the detection and monitoring of therapeutic responsiveness and minimal residual disease in leukemia patients and develop new clinical approaches to employ such data in therapeutic decision making and clinical trial design. (4) To maintain and expand tissue repositories of highly characterized leukemia samples from uniformly treated Southwest oncology Group patients to promote Intergroup and external fundamental scientific collaborations and to perform continued critical prospective and retrospective correlative biologic studies. (5) To utilize scientific information generated from Intergroup and collaborative studies to assist the leukemia committee in the development of new and more effective treatment regimens.

**Technical Approach:** The Southwest Oncology Group repositories are banks of extremely valuable leukemia samples which are made available to researchers who are studying various biological parameters and therapeutic diseases.

**Progress:** This protocol remains open to enrollment, with no patients enrolled.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200084	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9921: Adjuvant Androgen Deprivation versus Mitoxantrone plus Prednisone plus Androgen Deprivation in Selected High Risk Prostate Cancer Patients Following Radical Prostatectomy, Phase III		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 9/26/2000 - Jan 2002	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** This study will evaluate overall survival using adjuvant systemic therapy in high risk localized prostate cancer patients following radical prostatectomy. Disease-free survival will also be evaluated. Patients will be randomized to one of the following two treatment arms: (A) Casodex, + Zoladex, (B) Novantrone/Prednisone followed by Casodex, + Zoladex. This study will also compare qualitative and quantitative toxicity between the two study arms.

**Technical Approach:** This study compares standard hormonal therapy after prostate cancer surgery to standard therapy plus chemotherapy to determine the best way to prevent relapse. Subjects will be randomized to receive either Treatment 1, Hormonal Therapy which consists of Zoladex, subcutaneous injection once every 12 weeks for two years or Treatment 2, Hormonal Therapy plus Mitoxantrone plus Prednisone which consists of Zoladex subcutaneous injection once every 12 weeks for two years, Casodex taken orally once a day for two years, Mitoxantrone, IV once every 21 days for 126 days (6 cycles) and Prednisone, taken orally twice a day for 126 days. Following study completion, subjects will be followed every 6 months for two years to assess response.

**Progress:** This protocol is open to patient entry, with thirteen patients enrolled to date. Five patients continue to receive study treatment; the remaining eight patients continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202074	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S9925 Lung Cancer Specimen Repository Protocol, Ancillary		
<b>Principal Investigator:</b> MAJ Jasmine T. Daniels, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 9/24/2002 - Nov 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** (1) To establish a central lung cancer specimen repository to serve as a resource for current and future scientific studies. (2) To utilize Southwest Oncology Group clinical database to perform clinic pathologic correlation with the results of those studies. (3) To test new hypotheses as they emerge.

**Technical Approach:** Patients enrolled into select other SWOG lung cancer studies will be asked to consent to this study as well. Tissue samples will be obtained and stored.

**Progress:** This protocol is a companion study to other SWOG lung cancer treatment trials and remains open to patient entry, with three patients enrolled at MAMC; all now deceased.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204073	<b>Status:</b> Ongoing
<b>Title:</b> A Multicenter, Randomized, Phase III Study of Rituximab versus Iodine I 131 Tositumomab Therapeutic Regimen for Patients with Relapsed Follicular Non-Hodgkin's Lymphoma, Protocol CCBX001-049		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Maricela Contreras, MC; COL Marc G. Cote, MC; LTC Antonio G. Balingit, MC; Jane E. Besich-Carter, BS, BCNP		
<b>Start - Completion:</b> 7/26/2004 - Jun 2016	<b>Funding:</b> Corixa Corporation via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** (1) To compare the event-free survival, as assessed by a Masked Independent Randomized Radiographic and Oncologic Review (MIRROR) Panel, of patients treated with rituximab to that of patients treated with the Iodine I-131 Tositumomab therapeutic regimen in patients who have had at least one, but no more than two, prior therapies for follicular non-Hodgkin's lymphoma (NHL). (2) To compare confirmed response rates, durations of response, time to next treatment, and progression-free survival of patients treated with rituximab to that of patients treated with the Iodine I-131 Tositumomab therapeutic regimen in patients who have had at least one, but no more than two, prior therapies for follicular NHL, as assessed by a MIRROR panel, to compare overall survival in these two treatment groups, and to assess and compare the safety of rituximab and Iodine I-131 Tositumomab when administered to this patient population. (3) To summarize safety and efficacy outcomes during follow-up after subsequent therapy for NHL for patients in both arms who receive additional therapy.

**Technical Approach:** This is a multicenter, randomized, Phase 3 trial to compare rituximab and the Iodine I 131 Tositumomab therapeutic regimen in the treatment of subjects with follicular non-Hodgkin's B-cell lymphoma. Randomization will be stratified by prior rituximab treatment, first versus second relapse, and region, (US or outside the US). In Arm A, subjects will receive 375 mg/m<sup>2</sup> of rituximab as an IV infusion once weekly for 4 weeks. In Arm B, subjects will undergo a two phase treatment. In the dosimetric phase, subjects will receive an infusion of unlabeled Tositumomab (450mg) immediately followed by an infusion of 5 mCi (0.18 GBq) of Iodine I 131 Tositumomab (35 mg.) Whole body gamma camera scans will be obtained 3 times after the dosimetric dose. A patient-specific administered activity of Iodine I 131 Tositumomab will be calculated to deliver the desired total body dose of radiation (65 or 75 cGy).

In the second phase (therapeutic dose), subjects in Arm B will receive an infusion of unlabeled Tositumomab (450mg) immediately followed by infusion of the patient-specific activity of Iodine I 131-conjugated Tositumomab (35 mg.) Thyroid blockade will be implemented 24 hours prior to the dosimetric dose and continued for 14 days following. Hematology and serum chemistry will be measured for safety assessments weekly (hematology) and approximately monthly (chemistry) through Week 13, then at scheduled study follow up visits. Approximately 506 subjects will be randomized in the trial, and about 6 will participate at MAMC. The study will be conducted in the Hematology and Oncology Clinic in collaboration with the Nuclear Medicine Service. Subject accrual will continue for about 2 years. Subjects will be followed for response and safety measurements at weeks 7 and 13 and every 3 months for the first and second year, every 6 months for the third year, annually for the fourth and fifth years, then for long term follow up for survival, safety, and additional therapy data through year ten. After subsequent NHL therapy, follow up will assess tolerance of next anti-lymphoma therapy, development of NDS/AML, HAMA, or

hypothyroidism, unexpected safety issues, and death.

The primary analysis is the intent to treat comparison of event-free survival between treatment arms, which will be based on the MIRROR panel assessment of event-free survival. Secondary analyses will include the comparison of response rates and complete response rates (confirmed) and separate analyses will evaluate other responses, duration, time to next treatment, and overall survival. Secondary and exploratory analyses will include a stratified log rank test adjusting for stratification. Kaplan-Meier formula will be used to estimate duration curves and percentiles. Estimates and confidence limits will be calculated by the product limit method and Greenwood's formula for variance. Safety will be summarized within treatment arms and compared across treatment arms.

**Progress:** This protocol remains open to enrollment with no patients screened or enrolled during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205093	<b>Status:</b> Ongoing
<b>Title:</b> A Phase 3, Double-Blind, Placebo-Controlled Study of Maintenance Premetrexed plus Best Supportive Care versus Best Supportive Care Immediately Following Induction Treatment for Advanced Non-Small Cell Lung Cancer AND COMPANION STUDY Companion Translational Research Protocol		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 10/27/2005 - Aug 2010	<b>Funding:</b> Eli Lilly and Company via Henry M. Jackson Foundation	<b>Periodic Review:</b> 7/20/2006

**Study Objective:** (1) To compare maintenance therapy with Premetrexed plus best supportive care (BSC) versus placebo plus BSC, in terms of the overall survival time (OS) in patients with Stage IIIB (with pleural effusion and/or positive supraclavicular lymph nodes) or IV NSCLC who have not progressed during four cycles of platinum-based induction chemotherapy. (2) To compare the following between the randomized treatment arms: Time to event efficacy endpoints: Progression-free survival time (PFS), Time to objective progressive disease (TPD), Time to worsening of symptoms (TWS), Objective tumor response rate, Adverse events, and Changes in individual symptom scores and quality of life using the Lung Cancer Symptom Scale (LCSS).

**Technical Approach:** This is a phase 3, global, multicenter, randomized, double-blind, placebo-controlled study to compare maintenance therapy with Premetrexed plus BSC versus placebo in terms of overall survival time in patients with stage IIIB (with pleural effusion and/or positive supraclavicular lymph nodes) or stage IV NSCLC who have not progressed during four cycles of platinum-based induction chemotherapy. Eligible patients will be randomly assigned to receive Premetrexed plus BSC or placebo plus BSC. Patients in both treatment arms will receive folic acid, vitamin B12 supplements and dexamethasone. Each patient will undergo a treatment period and a follow-up period. The treatment period consists of 21 day treatment cycles. Patients will receive treatment (control or experimental) until objective disease progression. The follow-up period begins when the patient discontinues study treatment. Patients are to be followed with a periodic tumor response evaluation until objective disease progression. All patients will be followed until death or study closure.

The study will apply technology to evaluate intratumoral gene expression, followed by protein expression and DNA polymorphisms of key genes involved in the cellular transport, activation and cytotoxic activity of Premetrexed. All subjects entered into the clinical study will be invited to participate in the companion protocol. Samples will be shipped to the sponsor Eli Lilly and Company and will be stored for a maximum of 3 years after the companion study is completed and then the tissue samples will be destroyed.

**Progress:** This protocol remains open to enrollment with no subjects screened or consented during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206014	<b>Status:</b> Ongoing
<b>Title:</b> A Phase I/II Trial of Zometa in Patients with Monoclonal Gammopathy of Undetermined Significance (MGUS)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 6/6/2006 - July 2010	<b>Funding:</b> Oncotherapeutics via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10/16/2006

**Study Objective:** To determine the effect of zoledronic acid on bone mineral density (BMD) of lumbar spine, utilizing dual energy x-ray absorptiometry (DEXA) scan, among patients with MGUS with associated osteopenia/osteoporosis. The secondary objectives of this study are to: determine the effect of zoledronic acid on skeletal fractures in MGUS patients with osteopenia/osteoporosis, determine the effect of zoledronic acid on BMD of total hip, determine the effect of zoledronic acid on serum M-protein levels, determine the proportion of patients treated with zoledronic acid that develop multiple myeloma or other related malignancies, and determine the safety of the use of zoledronic acid in the treatment of MGUS patients with osteopenia/osteoporosis.

**Technical Approach:** This is an open label study designed to evaluate the efficacy and safety of zoledronic acid in MGUS patients with osteopenia/osteoporosis. A screening visit will be conducted within 14 days before baseline (baseline being prior to the administration of the first dose of study drug). At this visit, a medical history will be obtained and a complete physical examination will be performed including vital signs, weight, 12-lead electrocardiogram, and postero-anterior and lateral chest x-rays. Pre-study disease assessment will be performed, including bone mineral density (BMD) of lumbar spine, Karnofsky Performance Status (KPS), skeletal survey, bone marrow aspirate and biopsy (patients will be required to have this procedure if bone marrow aspirate and biopsy has never been performed to rule out the possibility of malignancy), serum and urine protein electrophoreses. The bone marrow aspirate and biopsy will be evaluated for degree of plasma cell involvement. Clinical laboratory tests including hematology, clinical chemistry (including electrolytes, calcium, magnesium and random glucose), liver tests, urinalysis, and serum pregnancy tests for women of child-bearing potential will also be performed at the Screening visit. Patients who meet the eligibility requirements as assessed at the Screening visit will be enrolled in the study. Zoledronic acid at 4 mg will be administered intravenously every 6 months over a period of 12 months. Patients are to attend a Final study visit. Procedures to be conducted at this visit include a complete physical examination, adverse event assessment, vital signs, Karnofsky performance status assessment and clinical chemistry.

**Progress:** This protocol opened to patient entry in June 2006; no subjects have been screened or enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205016	<b>Status:</b> Terminated
<b>Title:</b> A Phase II Multicenter, Randomized, Double-blind, Placebo-controlled Dose-Ranging, Parallel Group Study of the Safety and Efficacy of the Oral Neurokinin-1 Receptor Antagonist, GW679769, When Administered as 50mg, 100mg, and 150mg Oral Tablets in Combination with Ondansetron Hydrochloride and Dexamethasone for the Prevention of Chemotherapy-Induced Nausea and Vomiting in Cancer Subjects Receiving Moderately Emetogenic Chemotherapy		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 2/28/2005 - Jan 2007	<b>Funding:</b> GlaxoSmithKline via Henry M. Jackson Foundation	<b>Periodic Review:</b> 11/3/2006

**Study Objective:** Primary objectives: (1) To determine the optimal dose of oral GW679769 when administered in combination with ondansetron hydrochloride and dexamethasone for the prevention of vomiting during the first 120 hours in subjects receiving their first cycle of moderately emetogenic chemotherapy. (2) To determine the optimal dose of oral GW679769 when administered in combination with ondansetron hydrochloride and dexamethasone for the prevention of nausea during the first 120 hours in subjects receiving their first cycle of moderately emetogenic chemotherapy.

Secondary objectives: (1) To determine the safety of oral GW679769 at various dose levels when administered in combination with ondansetron hydrochloride and dexamethasone in subjects receiving their first cycle of moderately emetogenic chemotherapy. (2) To quantify the impact on daily life activities of oral GW679769 when administered in combination with ondansetron hydrochloride and dexamethasone during the first 120 hours in subjects receiving their first dose of moderately emetogenic chemotherapy. (3) To evaluate the population pharmacokinetics and pharmacodynamics (PK/PD) of oral GW679769 and its active metabolites when administered in combination with ondansetron hydrochloride and dexamethasone in subjects receiving their first cycle of moderately emetogenic chemotherapy.

**Technical Approach:** This trial is a double-blind, randomized, placebo-controlled, dose-ranging, parallel group study of the safety and efficacy of the oral neurokinin-1 receptor antagonist GW679769. At MAMC, the study will be conducted by the Hematology/ Oncology service with up to 20 subjects enrolled out of a total of 708 subjects in the study overall. Subjects scheduled to begin chemotherapy with a moderately emetogenic regimen will be consented and screened in the oncology service. On day 1 prior to the first chemotherapy cycle, subjects will be administered ondansetron hydrochloride (8mg or 16 mg), intravenous Dexamethasone (8mg) and an oral dose of GW679769 investigational produce (active or placebo). Subjects in groups 1, 2, 3, 4, or 5 will receive a second dose of oral ondansetron hydrochloride 8 hours following the initial dose. Subsequent dose or doses of ondansetron hydrochloride will be administered bid on days 2 and 3. For treatment group 6, the initial daily dose of ondansetron hydrochloride for days 1, 2 and 3 will be 16mg, followed by a second daily dose of ondansetron hydrochloride placebo. For study groups 1, 2, 3, 4 and 6, GW679769 will be administered once daily on study days 2 and 3 at the same dose as day 1. Subjects randomized to group 5 will receive a single active dose of GW679769 on day 1, and receive a single daily dose of GW679769 placebo on days 2 and 3. For study subjects who are receiving a taxane based therapy, Dexamethasone will not be given according to protocol, but will be given according to MAMC standard procedure for that specific chemotherapy regimen.

**Progress:** This protocol closed to enrollment with no subjects enrolled at MAMC. A final site close out visit was conducted in November 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 205087	<b>Status:</b> Suspended
<b>Title:</b> A Phase II, Open Label, Multi-center Study of EP2101 Therapeutic Vaccine in Patients with Stage IIb, Stage IV, or Recurrent Non-Small Cell Lung Cancer (NSCLC)			
<b>Principal Investigator:</b> LTC David E. McCune, MC			
<b>Department:</b> Medicine/Hematology & Oncology			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC Mark L. Nelson, MC			
<b>Start - Completion:</b> 9/21/2005 - Jul 2010		<b>Funding:</b> Epimmune via Henry M. Jackson Foundation	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** (1) To compare the overall survival of patients with stage IIb, IV, or recurrent non-small cell lung cancer treated with EP2101 therapeutic vaccine to a concurrent non-HLA-A2 observation group and historical controls. (2) To evaluate the safety of EP2101 therapeutic vaccine. Secondary: (1) To determine progression-free survival time in patients treated with EP2101 therapeutic vaccine. (2) To determine the frequency, magnitude, and breadth of cytotoxic and helper T-Cell responses to EP2101 vaccine epitopes.

**Technical Approach:** At MAMC, the study will be conducted by the Hematology/Oncology Service with up to 12 MAMC subjects expected to enroll, about 6 in the vaccine group and 6 in the observational group. A total of 168 subjects may be enrolled in the study overall. Patients who qualify will be consented to have their HLA type tested. Patients who do not qualify for the vaccine portion of the trial will be consented for the observational arm if they are interested. They will have a baseline medical history and physical, QOL, laboratory testing including CBC, chemistry, urinalysis and pregnancy test if applicable. Observational patients will be seen at Wk9, Wk18, Wk22, Mo6, Mo7, Mo9, Mo12, then every three months for years 2 and 3, and annually for years 4 and 5. Visits will include QOL, con meds, disease progression and survival status.

Patients who qualify for the vaccine arm of the trial (HLA type A2) will be consented and have the following pre-study assessment: complete medical history and physical exam, ECOG status performance, concomitant medications, laboratory testing including CBC, chemistry, ANA (autoimmunity), urinalysis and pregnancy testing if applicable, ophthalmic exam, disease assessment by CT or MRI scan, and Quality of Life (QOL) questionnaire. These patients will also be referred out to another facility to have leukapheresis performed, or have a 215 ml blood sample collected using a pediatric blood unit collection bag, to submit for immunogenicity and helper T-cell assays. Patients will receive the study vaccine once every three weeks for 6 cycles, for a total of 18 weeks of treatment. Patients will be monitored by the research nurse in the clinic for observation for 60 minutes after each vaccine, to assess for adverse events. At Wk 9 and 18, patients will have disease assessments done by CT or MRI, QOL, and laboratory tests including urinalysis, ANA, and blood collected for immunogenicity and helper T-cell assays. After treatment, patients will be followed at WK 22 and Mo7 for physical exam and ECOG score, laboratory tests including CBC and chemistry, adverse event and con med assessment and survival status. In addition, at Mo6, Mo 9 and Mo12, assessments will include disease progression monitored with CT or MRI, QOL, and laboratory tests including urinalysis, ANA, and blood collected for immunogenicity and helper T-cell assays. Long term follow up assessment of survival status will be scheduled every three months for years 2 and 3, then annually for years 4 and 5.

Toxicities will be graded at each study visit according to the National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0. Patients will be withdrawn from treatment for > Grade 2 toxicity of allergic reaction, hypersensitivity, autoimmune reaction or vasculitis, or for >



Grade 3 cytokine-like release reaction or local skin reaction. The study will be placed on hold for safety review if toxicities exceed the safety criteria outlined on Pg 37 of the protocol.

**Progress:** This protocol closed to enrollment with three subjects consented and enrolled. One subject had disease progression and is no longer on the treatment arm; two subjects remain on treatment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 205070	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II Study Using Alemtuzumab Combined with Fludarabine for the Treatment of Relapsed/Refractory B-cell Chronic Lymphocytic Leukemia (B-CLL)			
<b>Principal Investigator:</b> LTC David E. McCune, MC			
<b>Department:</b> Medicine/Hematology & Oncology			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwicz, MC			
<b>Start - Completion:</b> 7/13/2005 - Jun 2010	<b>Funding:</b> Berlex Laboratories via Henry M. Jackson Foundation		<b>Periodic Review:</b> 4/20/2006

**Study Objective:** The primary objective is to evaluate complete response rate in patients receiving combination treatment with Alemtuzumab and fludarabine. The secondary objectives are to evaluate overall response rate, survival at 1 year, time to progression, duration of response, adverse event profile, minimal residual disease and lymphocyte and lymphocyte subset recovery.

**Technical Approach:** This is a Phase II, open label trial of the combination of alemtuzumab and fludarabine for the treatment of relapsed/refractory B-cell chronic lymphocytic leukemia. This study will evaluate the response rate, survival, time to progression, duration of response lymphocyte subset recovery and safety profile of the combination of subcutaneous alemtuzumab and fludarabine. Patients will receive four 28-day cycles of treatment with alemtuzumab 30 mg subcutaneously followed by 25mg/m<sup>2</sup> IV of fludarabine, daily on days 1 through 5. At the end of 4 cycles, patients will have an interim assessment to determine response to treatment. This will include radiographs as needed and a bone marrow biopsy. Minimal residual disease assessment will be performed on the marrow samples. Patients who have responded or have stable disease will receive two additional cycles of chemo as in Cycles 1-4. After treatment is completed, subjects will be followed up every 6 months for disease assessment, CMV, and flow cytometry for lymphocyte subset analysis to be done monthly until CD4 and CD8 T cell counts recover to >200 cells/uL.

All patients will be prescribed Bactrim for PCP prophylaxis and famcyclovir for HSV prophylaxis starting with Day 1, and continuing for at least 2 months after treatment, or until CD4 counts are >200 cells/uL. Patients will be monitored for CMV status throughout the study and for 6 months after treatment. If patients become CMV positive they will receive appropriate anti-CMV therapy and may have study drug delayed until CMV treatment is complete. Growth factors may be used at the discretion of the investigator for Grade 3 or 4 neutropenia, however TPO and pegfilgrastim will not be allowed. Toxicities will be graded at each study visit according to the National Cancer Institute (NCI) Common Toxicity Criteria (CTC) Version 3.0 Safety will be assessed through physical examinations and laboratory assessments at each study visit.

**Progress:** This protocol was closed to enrollment at MAMC due to a lack in screening and enrollment activity.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206126	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II Trial of Imatinib (Gleevec) Plus Gemcitabine In Patients With Ovarian Carcinoma Who Have Failed At Least One Prior Chemotherapy		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; MAJ Jasmine T. Daniels, MC; MAJ Richard D. Reed, MC		
<b>Start - Completion:</b> 11/20/2006 - Oct 2011	<b>Funding:</b> ACOSOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To evaluate the cytostatic, anti-tumor activity of the combination of Gleevec™ (Imatinib Mesylate) and gemcitabine via progression-free survival for at least six months in subjects with recurrent or persistent epithelial ovarian or primary peritoneal carcinoma. (2) To assess the tumor response rates using modified SWOG criteria to the combination of Gleevec™ (Imatinib Mesylate) and gemcitabine in subjects with relapsed ovarian cancer who have failed at least one prior chemotherapy treatment. (3) To determine the safety and tolerability via frequency and severity of adverse effects of combination Gleevec™ and gemcitabine in this cohort of subjects as assessed by CTC. (4) To determine the distribution of the overall survival. (5) To estimate the clinical response rate (partial and complete response as defined under the modified SWOG criteria). (6) To assess the effects of prognostic variables: initial performance status, platinum sensitivity, and mucinous (or clear cell) histology on progression-free survival overall.

**Technical Approach:** This is a Phase II, single arm, open label treatment study to evaluate the tumor response rate to the combination of Gleevec and Gemcitabine for treatment of women who have failed at least one prior chemotherapy regimen containing platinum. 60 subjects are expected to enroll to achieve a goal of 56 evaluable subjects, with 20 subjects expected to enroll at MAMC. Women will be recruited during regular visits to the Oncology Clinic; those appearing eligible will be consented and screened. Those who qualify will be given a combination of oral Gleevec and IV Gemcitabine, over a 21 day cycle, for as long as they respond and are able to tolerate the combination. Subjects experiencing side effects may receive supportive care with growth factors or antiemetics as appropriate or have their dose modified per protocol. Subjects will be followed after each cycle by physical exams, laboratory assessments including CA-125 tumor marker, and by review of adverse events and cancer-related symptoms. Tumor assessments will be done every other cycle by CT or MRI. Subjects removed from treatment will be followed every three months by clinic visit or phone contact for up to five years to determine time to progression and survival rates.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 26 September 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204114	<b>Status:</b> Ongoing
<b>Title:</b> A Phase II Trial of Weekly Docetaxel plus Every 3-Week Carboplatin in Patients with Stage IIIB/IV Non-small Cell Lung Cancer, Protocol GIA 12156		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 10/27/2004 - Nov 2007	<b>Funding:</b> Aventis Pharmaceuticals, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** Primary Objective is to determine overall response rate for patients with advanced non-small cell lung cancer treated with weekly docetaxel 35 mg/m<sup>2</sup> on days 1 and 8 plus carboplatin (AUC 6) on day 1 every 21 days. Secondary Objectives are to determine the 1-year survival rate, the median overall survival rate, and to evaluate the safety and toxicity associated with this regimen.

**Technical Approach:** This trial is a two-stage, phase II study of weekly docetaxel 35 mg/m<sup>2</sup> infused on days 1 and 8 plus carboplatin (AUC 6) on day 1 only, repeated every 21 days (cycle) in patients with stage IIIB or IV advanced non small cell lung cancer who have not received prior chemotherapy. 4-6 MAMC subjects are expected to be enrolled. A total of 29 patients may be enrolled in the study overall. Physical examination and history, baseline tumor assessments, ECOG performance status, CBC, serum chemistry, EKG, and serum HCG as appropriate, will be evaluated prior to study treatment. A minimum of two courses of treatment will be given unless there is progression of disease or significant adverse reactions occur. Patients will be monitored after every two cycles (6 weeks) for tumor response using standard radiographic imaging. Objective response will be evaluated using the RECIST criteria (Response Evaluation Criteria In Solid Tumors). Clinical and laboratory toxicities will be assessed and graded according to the NCI Common Toxicity Criteria, version 2.0. Appropriate supportive care treatment will be administered. Chemotherapy dose adjustments will be made based on the organ system exhibiting the greatest degree of toxicity. Eligible patients will be treated for 2 additional cycles after best documented tumor response. All patients will be followed after treatment at defined intervals for survival data.

The primary endpoint of this study is overall response rate (complete response plus partial response). Ten patients will be enrolled into the first stage. If at least 1 patient responds, 19 additional patients will be enrolled into the second stage of the study. If at least 5 of 29 evaluable patients exhibit an objective response at the end of the second stage, the conclusion will be that this regimen is worthy of further study. Secondary endpoints will be reported for the 1-year survival rate, the median overall survival rate, evaluations of safety and toxicity associated with this regimen. The primary efficacy analysis will be conducted on all patients who receive the study drug. Objective tumor response rate along with exact 95% binomial confidence intervals will be calculated. Time-to-event outcomes including 1-year survival, time to disease progression, and duration of response will be estimated using the Kaplan- Meier product limit method. Median and quartile estimates for each time-to-event outcome will be obtained from the Kaplan-Meier estimates.

**Progress:** This protocol closed to enrollment with one subject enrolled who remains in follow-up for survival information only. There are no unreported serious adverse events at the time of this report.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204006	<b>Status:</b> Terminated
<b>Title:</b> A Phase III, Randomized, Double-blinded Efficacy and Safety Study of Three Doses of TAS-108 Administered Orally in Postmenopausal Patients with Locally Advanced or Locally Recurrent Inoperable or Progressive Metastatic Breast Carcinoma Following Standard First Line Endocrine Therapy, Protocol Number TAS108-0004		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; MAJ Jasmine T. Daniels, MC; M. Rick Rutledge, MS		
<b>Start - Completion:</b> 1/20/2004 - Jan 2006	<b>Funding:</b> Taiho Pharmaceutical Co., Ltd. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 11/22/2005

**Study Objective:** (1) To determine the efficacy of TAS-108 administered orally once daily at 40 mg, 80 mg, and 120 mg in postmenopausal patients with locally advanced or locally recurrent inoperable or progressive metastatic ER/PgR positive breast carcinoma who have previously responded to a standard first line endocrine therapy. (2) To evaluate the safety of TAS-108 administered on this schedule. (3) To investigate the comparative concentrations of TAS-108 and its metabolite in tumor tissue and blood at steady-state. (4) To determine the time to progression of TAS-108 administered on this schedule.

**Technical Approach:** This is a phase II, randomized, double-blinded study of TAS-108 administered orally once daily at 40 mg, 80 mg, or 120 mg to be carried out at multiple study sites. The statistical calculation of the sample size will be based on a single arm study design and the study will use this same number for each dose group. It is exactly the same as three identical studies, using 40 mg, 80 mg, and 120 mg to be conducted at the same study sites at the same time. The efficacy and safety results from each dose group will only be evaluated independently and clinically, but not compared biostatistically. Patients will be enrolled to the 40 mg, 80 mg, and 120 mg dose levels randomly until the first stage number is met for each dose group. Depending on the randomization schedule, the enrollment completion for each group may be far apart. The enrollment will be put on hold for each respective dose group until the data to be evaluated meets the preset criterion to proceed to the second stage. Since each dose group will be evaluated separately and independently, the time point of meeting the preset criteria and allowing patients to proceed into the second stage of the study will most likely be different for the three dose groups. When the enrollment into the second stage of the study for each dose group is completed, analysis for each group will be performed independently according to the analysis plan. In this study, one course equals 28 days of treatment. Patients will receive study treatment until (a) there is evidence of disease progression or (b) the patient develops unacceptable toxicity to TAS-108 or (c) the patient withdraws informed consent.

**Progress:** This protocol was terminated by the PI in July 2006, with no subjects enrolled. Only one patient had met the appropriate inclusion criteria, but she decided not to participate in the study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204044	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III Study of Delayed vs. Immediate Second-line Therapy with Docetaxel after Gemcitabine + Carboplatin in Advanced Non-Small Cell Lung Cancer, Protocol Number B9E-US-S245		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 4/1/2004 - Apr 2007	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** Primary Objective is to test the value in terms of overall survival of immediate sequential therapy with docetaxel compared to traditional second-line therapy with docetaxel at the time of progression after standard Carboplatin and Gemcitabine in patients with stage IIIb and IV non-small cell lung cancer. Secondary Objectives: (1) to assess the response rate and time to disease progression, (2) to compare toxicity in these two groups and (3) to compare quality of life using the LCSS patient scale.

**Technical Approach:** This is a multicenter open-label randomized phase III trial to evaluate the respective response rates, time to disease progression, survival time, toxicity, and quality of life of immediate sequential therapy with docetaxel compared to traditional second-line therapy with docetaxel at the time of disease progression, after standard Carboplatin and gemcitabine in subjects with stage IIIb and IV non-small cell lung cancer (NSCLC). Up to 5 MAMC subjects may participate, with 550 subjects in the overall study. Duration of individual participation will be up to 36 months. The study will enroll chemotherapy-naïve subjects whose NSCLC is advanced at diagnosis or has recurred or progressed following surgical treatment and/or radiation therapy, and who meet additional eligibility criteria.

Following screening, eligible subjects will receive the first phase of treatment with gemcitabine and Carboplatin chemotherapy on Day 1 and Day 8 every 21 days, followed by one week of rest, for four cycles. Safety and response will be monitored. Disease restaging will be done at the end of first phase treatment. Subjects with complete or partial response or stable disease after initial therapy will be rescreened and eligible subjects will be randomized (1:1) to the second phase treatment with immediate or delayed docetaxel. Subjects found to have progressive disease after initial therapy or who discontinue prior to completion of 4 cycles will be followed for survival data. Subjects randomized to delayed therapy will be monitored every three weeks prior to treatment. Radiological imaging of tumor sites will be performed every 3 months or as clinically indicated. With evidence of disease progression, subjects begin treatment with docetaxel. Subjects randomized to receive immediate sequential docetaxel and subjects initiating traditional treatment after progression will receive docetaxel on Day 1 every 3 weeks for a maximum of 6 cycles. Response and safety will be monitored. Subjects who complete the protocol or who discontinue study chemotherapy early will be followed at protocol intervals until progression or death. The primary endpoint is survival and will be measured from time of randomization to date of death for all randomized subjects. Secondary endpoints of response rates, time to progression, toxicity, and LCSS will be compared between regimens. An independent Data Safety Monitoring Board will assess safety at the time of formal interim analysis, planned when 50% of subjects in each docetaxel treatment arm have 1) died, 2) are lost to follow up prior to 24 months, or 3) have been followed up for at least 24 months.

**Progress:** This protocol closed to enrollment with seven subjects consented. Five subjects are deceased due to non-study related deaths and two patients continued to be followed during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204096	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Open-Label Study of PROCrit® (Epoetin Alfa) Initiated at 40,000 Units Every Week Versus 80,000 Units Every Two Weeks In Anemic Patients With Cancer Receiving Chemotherapy, Protocol PR03-27-064		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 9/15/2004 - Sep 2006	<b>Funding:</b> OrthoBiotech via Henry M. Jackson Foundation	<b>Periodic Review:</b> 6/28/2005

**Study Objective:** Primary Objective: To compare end of study hemoglobin (Hb) levels of subjects receiving epoetin alfa (PROCrit®) 40,000 units administered subcutaneously once every week with those receiving 80,000 units every two weeks, in anemic patients with cancer diagnosis and receiving chemotherapy. Secondary Objectives: To assess Hb response, time to Hb response, transfusion requirements, and safety of the two dose regimens.

**Technical Approach:** This is a randomized, open-label, multi-center trial that will compare efficacy and safety of two dose regimens of Procrit® (Epoetin Alfa), 40,000 units administered subcutaneously once every week with 80,000 units every two weeks, in anemic patients with non-myeloid cancer diagnosis and receiving chemotherapy. 280 patients who meet all inclusion and exclusion criteria will be enrolled and randomized at approximately 75 study centers to one of the two treatment groups in a 1:1 ratio. The enrollment phase is expected to last 15 months. All patients will be followed weekly until two weeks after the last dose of Epoetin Alfa, or up to a maximum of 13 weeks on study (12 weeks of study drug). The starting doses may be adjusted per protocol based on Hb response. If chemotherapy is completed before week 12, one final dose of Epoetin Alfa will be administered on the assigned schedule at the end of the final cycle of chemotherapy. Unless there is a contraindication, all patients will receive iron supplementation (ferrous sulfate 325mg by mouth daily or an equivalent). Transfusions may occur as needed for patient care. At MAMC, a hemoglobin value of less than 8.0 g/dL or a clinical judgment based on symptoms will be the trigger event for blood transfusion. Subjects will be monitored weekly during treatment and at study completion for blood pressure, hematologic response (hemoglobin and hematocrit), adverse events, concomitant medications and transfusions. Physical exam with vital signs, ECOG Performance Status, and laboratory testing as completed at screening will be repeated at the end of study. The primary efficacy endpoint is end of study Hb, which will be analyzed for the per-protocol and intent to treat populations. Safety analyses will describe adverse events, laboratory values, physical exam, vital signs and ECOG status and will include all randomized subjects receiving at least one dose of study medication.

**Progress:** This protocol closed to enrollment 16 May 05, and closed as a study site 22 November 2006, with eight subjects screened, two screen failures, six enrolled, four completed the study, one was removed when relocated, and one subject removed for what was thought to be a thrombosis, which turned out not to be so and was not reported as an event. No internal serious adverse events were reports.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202083	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Phase III Trial of Gemzar versus Doxil with Crossover Treatment Option for Patients with Platinum-Resistant Ovarian, Fallopian Tube or Primary Peritoneal Cancer Undergoing Second or Third-Line Chemotherapy, Protocol Number: B9E-US-S301		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 8/14/2002 - Jul 2005	<b>Funding:</b> Lilly via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** (1) To compare progression free survival in patients with platinum-refractory epithelial ovarian, Fallopian tube, or primary peritoneal carcinoma who have failed two or less prior regimens of chemotherapy that are treated with Doxil or Gemzar. (2) To compare response rate, duration of response, time to treatment failure, survival, and quality of life in patients with platinum-refractory epithelial ovarian, Fallopian tube, or primary peritoneal carcinoma who have failed two or less prior regimens of chemotherapy who are treated with Doxil or Gemzar.

**Technical Approach:** At MAMC there are expected to be 5-10 patients enrolled during approximately one year.

Patient screening will include written informed consent, medical history and demographics, tumor assessment by exam or imaging, FACT-O questionnaire, Zubrod Performance Status, LVEF, chemistry and hematology, CA-125 tumor marker, contraceptive status and serum pregnancy test. Patients on the Doxil arm will be treated with 50 mg/m<sup>2</sup> on Day 1 of each 28 day cycle. Treatment will continue for two cycles after a complete response, or until a cumulative maximum dose of 500 mg/m<sup>2</sup> has been given. Patients on the Gemzar arm will be treated with 1000mg/m<sup>2</sup> on Days 1 and 8 of a 21 day cycle. Treatment will continue for up to two cycles after complete response is attained. For patients with stable disease there is no maximum number of Gemzar cycles. Patients who have progressive disease may cross over to the other treatment arm if they are eligible. Patients will be monitored every cycle for toxicities, chemistry, hematology, performance status and CA-125 tumor staging. Dose adjustments will be made based on NCI toxicity criteria. FACT-O Quality of Life questionnaire will be administered every other cycle, and tumor assessment imaging will be performed every 12 weeks. Primary efficacy will be evaluated using Kaplan-Meier techniques. Secondary efficacy analysis will be conducted on response rate, duration of response, time to treatment failure, survival and quality of life. Response rates from the two treatment arms will be compared using Fisher's Exact test. Summaries on toxicity parameters will be provided.

**Progress:** This protocol closed to patient entry in May 2004, with four patients enrolled. Two patients are deceased and two continued to be followed at MAMC during FY06. No patients are receiving treatment. The protocol remains ongoing pending closeout of the database by the study sponsor.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204107	<b>Status:</b> Suspended
<b>Title:</b> CTSU ACOSOG-Z9001, A Phase III Randomized Double-blind Study of Adjuvant STI571 (Gleevec™) Versus Placebo in Patients Following the Resection of Primary Gastrointestinal Stromal Tumor (GIST)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 11/1/2004 - Aug 2008	<b>Funding:</b> ACOSOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 12/12/2006

**Study Objective:** Primary Objective: To ascertain whether patients with resected primary GIST who are randomized to the STI571 Arm have longer recurrence-free survival as compared to the patients randomized to the Placebo Arm. Secondary Objectives: (1) To ascertain whether patients with resected primary GIST who are randomized to the STI571 Arm have longer survival as compared to the patients randomized to the Placebo Arm. (2) To obtain from patients with GIST: tumor tissue (before therapy with STI571 and if the patient develops recurrence), blood specimens (before therapy with STI571), and serum specimens (before therapy with STI571, after completing therapy with STI571, and if the patient develops recurrence) for scientific correlative analyses. (3) To assess the safety/efficacy of oral STI571 therapy in the adjuvant setting.

**Technical Approach:** Patients will be randomized into one of two groups; four 100mg capsules for a total of 400mg of the experimental drug or placebo by mouth every day for 1 year. Weight should be measured at home two times per week and the physician called if there is a weight change by more than 4 pounds from the weight taken at the last clinic visit. Patients will have a physical exam before the start of drug or placebo and then seen in the clinic weekly the first 2 weeks, at weeks 4, 6 and 8, at 3, 4, 5 and 6 months, every 3 months until year 2, every 6 months until year 5 and then every year until death.

Tumor tissue will be sent to a central pathologist to confirm the diagnosis of GIST and if it has a protein called Kit, as the presence of this protein is required for the Gleevec to work. If the tissue sample results show that the tumor is not GIST or if the Kit protein is not there, the study drug will be stopped and patients will have a physical examination and a blood test about 30 days after the study drug is stopped. These patients will continue to be contacted by phone every 3 months for 1 year, every 6 months for 3 years, and then every year until death.

**Progress:** This protocol remains open to enrollment, with one subject enrolled and remained on active treatment during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202114	<b>Status:</b> Ongoing
<b>Title:</b> CTSU CALGB 40101, Cyclophosphamide and Doxorubicin (CA) (4 VS 6 Cycles) versus Paclitaxel (4 VS 6 Cycles) as Adjuvant Therapy for Women with 0-3 Positive Axillary Lymph Nodes: A 2X2 Factorial Phase III Randomized Study		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 11/14/2002 - Oct 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/22/2006

**Study Objective:** Primary Objectives: (1) To determine the equivalence of paclitaxel given every two weeks with CA given every two weeks as adjuvant therapy for women with 0-3 positive axillary lymph nodes, for disease free survival. (2) To determine if longer therapy, 12 weeks, is superior to shorter therapy, 8 weeks, of either CA or paclitaxel for disease-free survival for women with primary breast cancer with 0-3 positive axillary lymph nodes.

Secondary Objectives: (1) To determine the equivalence of paclitaxel given every two weeks with CA given every two weeks, and the potential superiority of longer vs. shorter therapy, in relation to overall survival, local control (regardless of metastatic status) and time to distant metastases (regardless of local recurrence status) (2) Compare toxicities of short and long course CA and paclitaxel as adjuvant therapy for women with 0-3 positive axillary lymph node breast cancer (3) To determine the effect of long and short course CA and paclitaxel on the induction of menopause for pre-menopausal patients. (4) To assess the discrepancy of myelosuppression among the common MDR1 haplotypes in the CA treatment arm. (5) To assess the effect of MDR1 haplotypes on DFS adjusted for treatment. (6) Exploratory analysis of the effect of CYP3A5, CYP2Cs and CYP2B6 polymorphisms on DFS and toxicity.

**Technical Approach:** This is a randomized study and patients will be stratified according to menopausal status (premenopausal vs postmenopausal) and estrogen receptor (ER)/progesterone receptor (PR) status (ER and/or PR positive or unknown vs ER and PR negative). Patients are randomized to 1 of 4 treatment arms. Arm I: Patients receive doxorubicin IV over 10-15 minutes and cyclophosphamide IV on day 1. Treatment repeats every 21 days for 4 courses. Arm II: Patients receive doxorubicin and cyclophosphamide as in arm I. Treatment repeats every 21 days for 6 courses. Arm III: Patients receive paclitaxel IV over 1 hour once weekly for 12 weeks. Arm IV: Patients receive paclitaxel as in arm III for 18 weeks. Treatment in all arms continues in the absence of disease progression or unacceptable toxicity. Lumpectomy patients must then undergo radiotherapy. Mastectomy patients undergo radiotherapy at the discretion of the treating physician. Patients are followed every 6 months for 2 years and then annually for 15 years.

**Progress:** This protocol remains open to patient entry, with six patients enrolled. One patient is currently receiving active treatment and the other five continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202089	<b>Status:</b> Ongoing
<b>Title:</b> CTSU CALGB 49907, A Randomized Trial of Adjuvant Chemotherapy With Standard Regimens, Cyclophosphamide, Methotrexate and Fluorouracil - (CMF) or Doxorubicin and Cyclophosphamide - (AC), Versus Capecitabine in Women 65 Years and Older with Node Positive or Node Negative Breast Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 12/5/2002 - Jul 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** (1) To compare the effectiveness of standard chemotherapy (CMF or AC) with single agent Capecitabine with respect to disease-free survival in women 65 years and older with local and regional breast cancer. (2) To compare the effectiveness of standard chemotherapy regimens with Capecitabine with respect to overall survival.(3) To determine the effects of each treatment regimen on quality of life and physical function. (4) To assess the toxicity of each treatment program. (5) To study the adherence to an oral chemotherapy regimen in older patients.

**Technical Approach:** This study compares the oral anti-cancer drug Capecitabine to standard adjuvant therapy of Cyclophosphamide, Methotrexate and Fluorouracil, or Doxorubicin and Cyclophosphamide in women who have complete breast cancer surgery and are over 65 years old. The study will attempt to find a survival her forth difference in relapse rates or a quality of life.

**Progress:** This protocol is open to patient entry, with no patients enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204124	<b>Status:</b> Completed
<b>Title:</b> CTSU CALGB 80303, A Randomized Phase III Trial of Gemcitabine plus Bevacizumab (NSC #704865 IND #7921) Versus Gemcitabine plus Placebo in Patients With Advanced Pancreatic Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwicz, MC		
<b>Start - Completion:</b> 1/25/2005 - Oct 2008	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/19/2005

**Study Objective:** The primary objective is to determine if combination chemotherapy with Gemcitabine and Bevacizumab achieves superior survival compared to Gemcitabine and Placebo in patients with previously untreated advanced pancreatic cancer. Secondary objective is to compare response rates, duration of response, progression free survival, and toxicity of these two regimens in patients with advanced pancreatic cancer. Angiogenic biomarker studies are to measure baseline levels of VEGF and correlate with treatment outcome, to measure baseline and on treatment levels of additional growth factors that may be co- or counter-regulated with VEGF and correlate with response to treatment, to measure baseline and treatment levels of coagulation and endothelial cell activation markers and to generate protein expression profiles using a MALDI-TOF based platform from serum samples. Pharmacogenomic predictors outcome is to assess any differences in overall survival within the treatment arm (Gemcitabine+Bevacizumab), between the two VEGF genotypic groups: Group I denoted by individuals with CT or TT genotypes and Group 2 consisting of individuals with CC genotypes., to conduct an exploratory analysis of gene-toxicity, gene-response, and gene survival relationships. The clinical Economics of the study is to compare the effects of Gemcitabine+Bevacizumab versus Gemcitabine+ Placebo on resource utilization, cost, and utilities, and if applicable, to make estimates of marginal cost-utility.

**Technical Approach:** This study compares standard gemcitabine chemotherapy for advanced pancreatic cancer to standard therapy plus Bevacizumab, a monoclonal antibody directed at vascular endothelial growth factor. Eligible patients will be randomized to receive either Gemcitabine plus Bevacizumab or Gemcitabine plus placebo. Each treatment group receives therapy over a 28 day cycle. The study will compare response rates, toxicity and survival between the two treatments in an attempt to establish a new standard of care.

**Progress:** The protocol was reported completed at MAMC in April 2006 when the study closed to enrollment with one subject who enrolled during FY05, but died due to disease progression.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202088	<b>Status:</b> Ongoing
<b>Title:</b> CTSU E1A00 A Randomized Phase III Trial of Thalidomide (NSC #66847) Plus Dexamethasone versus Dexamethasone in Newly Diagnosed Multiple Myeloma		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 6/25/2002 - Jul 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/22/2006
<b>Study Objective:</b> 1) To evaluate the response rate and toxicity of thalidomide plus dexamthasone and dexamethasone alone in patients with newly diagnosed myeloma. 2) To study the effect of thalidomide on bone marrow microvessel density and angiogenesis grade and on the expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in the marrow.		
<b>Technical Approach:</b> Compare a standard treatment for myeloma, dexamethasone to dexamethasone plus thalidomide. The goal of the study is to see if there is any difference between the two with respect to response rate, complications and quality of life or survival.		
<b>Progress:</b> This protocol closed to patient entry in April 2003, with one patient enrolled who continued to be followed at MAMC during FY06.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204072	<b>Status:</b> Completed
<b>Title:</b> CTSU E3201 Intergroup Randomized Phase III Study of Postoperative Irinotecan, 5-Fluorouracil and Leucovorin vs Oxaliplatin, 5-Fluorouracil and Leucovorin vs 5-Fluorouracil and Leucovorin for Patients with Stage II or III Rectal Cancer Receiving Either Preoperative Radiation and 5-Fluorouracil or Postoperative Radiation and 5-Fluorouracil		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC Tommy A. Brown, MC; MAJ Jasmine T. Daniels, MC; LTC William B. Reece, MC; LTC John B. Halligan, MC		
<b>Start - Completion:</b> 8/2/2004 - May 2008	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/25/2005

**Study Objective:** (1) To compare the overall survival of patients treated with Irinotecan, 5-FU and Leucovorin versus those treated with Oxaliplatin, Leucovorin and 5-FU versus those treated with Leucovorin and 5-FU for patients with Stage II and III rectal cancer. (2) To compare sphincter preservation, tolerance of treatment and patterns of failure. (3) To prospectively assess rectal function using the Patient Bowel Function/Uniscale questionnaire and the FACT Diarrhea Subscale in patients treated with an adjuvant program of pelvic radiation therapy and chemotherapy. (4) To correlate TS< DPD and TP expression (key targets for 5-FU); retention of chromosome 18q alleles and MSI with TGFβ1RII mutation) (markers for 5-FU efficacy); and p53 gene mutation in tumor tissue specimens with treatment efficacy (5) To correlate tumor molecular prognostic markers (chromosome 18q allelic loss and MSI) with survival. (6) To determine physician preference in regard to the radiation-chemotherapy sequence in the Intergroup.

**Technical Approach:** The study compares standard adjuvant treatment for rectal cancer to two different chemotherapy combinations to see if any regimen is superior for survival or toxicities. All eligible patients with rectal cancer will be offered the study. Subjects will be offered one of three chemotherapy combinations: (1) 5-FU + Leucovorin, (2) 5-FU + Leucovorin + Oxaliplatin, or (3) 5-FU + Leucovorin + Irinotecan. Data will be collected on survival, toxicity, and relapse rates. Toxicity will be assessed at each patient visit. Data will be analyzed centrally by CTSU.

**Progress:** ECOG announced permanent closure of this protocol effective 28 October 2005, no patients enrolled at MAMC. This study has been redesigned and will soon open with a new study number for new patient accrual.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204043	<b>Status:</b> Ongoing
<b>Title:</b> CTSU IBCSG Trial 25-02, Tamoxifen and Exemestane Trial (TEXT), A Phase III Trial Evaluating the Role of Exemestane Plus GnRH Analogue as Adjuvant Therapy for Premenopausal Women with Endocrine Responsive Breast Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwicz, MC; LTC Tommy A. Brown, MC; LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 5/12/2004 - Feb 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006
<b>Study Objective:</b> Evaluate the worth of ovarian function suppression (achieved by long-term use of GnRH analogue) plus exemestane compared with GnRH analogue plus Tamoxifen for premenopausal women with steroid hormone receptor-positive early invasive breast cancer.		
<b>Technical Approach:</b> This trial compares two different types of hormonal therapy for the prevention of relapse after breast cancer surgery. Subjects may either receive no chemotherapy or commence chemotherapy at the same time that GnRH analogue is initiated. Eligible subjects will be randomized into one of two groups; surgery plus GnRH analogue and tamoxifen for 5 years or surgery plus GnRH analogue plus exemestane for 5 years.		
<b>Progress:</b> This protocol remains open to enrollment with one subject enrolled at MAMC, but had to be transferred to Swedish Hospital and Medical Center, Seattle, WA.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204035	<b>Status:</b> Ongoing
<b>Title:</b> CTSU NCIC CTG MA.27, A Randomized Phase III Trial of Exemestane Versus Anastrozole in Postmenopausal Women With Receptor Positive Primary Breast Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 5/12/2004 - Jan 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** Primary objective: Compare event free survival (EFS) between women treated with exemestane or Anastrozole as adjuvant therapy. Secondary objectives: (1) To compare overall survival(OS) of women treated with exemestane with that of those receiving Anastrozole as adjuvant therapy, (2) To compare the time to distant recurrence for women treated with exemestane with that for women receiving Anastrozole as adjuvant therapy, (3) To compare the incidence of new primary contra lateral breast cancer in the different treatment groups, (4) To compare the incidence of all clinical fractures and specifically hip and vertebral fractures in the different treatment groups, and (5) To compare cardiovascular morbidity and mortality (i.e. significant coronary heart disease, which includes myocardial infarctions and angina requiring percutaneous transluminal coronary angioplasty or coronary artery bypass graft, fatal and nonfatal strokes and all vascular deaths) between exemestane and Anastrozole.

Note: Study objectives looking at the use of Celecoxib in this patient population were discontinued, 17 Dec. 04.

**Technical Approach:** This study compares two different aromatase inhibitors in an attempt to establish standard of care for this type of breast cancer. Eligible subjects will be randomized to receive either Exemestane or Anastrozole. treatment period will be 5 years except in cases of unacceptable side effects or disease recurrence.

Note: The randomization in a double-blinded fashion to receive either Celecoxib or placebo was discontinued Dec 04, due to increased frequency of fatal and non-fatal cardiovascular events observed on the celecoxib arm of an NCI sponsored study of the prevention of colorectal polyps. mentioned protocol has discontinued giving celecoxib/placebo to enrolled subjects. due to concerns about the use of the Cox II inhibitor.

**Progress:** This protocol is closed to enrollment except for some sites that are performing specific sub-studies. Ten patients enrolled at MAMC, and remain in treatment or follow-up during FY06.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205071	<b>Status:</b> Terminated
<b>Title:</b> CTSU NSABP 80101 Phase III Intergroup Trial of Adjuvant Chemoradiation after Resection of Gastric or Gastroesophageal Adenocarcinoma		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; LTC William B. Reece, MC; LTC John B. Halligan, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> Never approved	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objective: To determine whether overall survival is prolonged in patients with resected gastric Adenocarcinoma who receive epirubicin, cisplatin, and infusional 5-FU (ECF) before and after infusional 5-FU plus radiotherapy (RT) when compared to those treated with bolus 5-FU and Leucovorin before and after infusional 5-FU plus RT. Secondary objectives. (1) To determine disease-free survival and distant recurrence rates (2) To prospectively assess whether expression of putative prognostic markers in the tumor correlate with overall survival (3) To prospectively assess whether specific germ line polymorphisms related to chemotherapy metabolism and resistance correlated with treatment-related toxicity and overall survival (4) To prospectively assess whether serum levels of various growth factors correlated with overall survival (5) To determine whether hospital procedure volume predicts recurrence-free and overall survival

### Technical Approach:

This is a randomized comparison of patients with completely resected gastric or gastroesophageal cancer who receive ECF before and after infusional 5-FU plus RT versus patients who treated with bolus 5-FU and Leucovorin before and after infusional 5-FU plus RT. The study will enroll 824 patients, male and female, age 18 and over, who have undergone complete resection of adenocarcinoma of the stomach or gastroesophageal junction. Up to 10 patients will participate at MAMC. Patients will be assessed at screening with history and physical exam, height, weight, vitals, laboratory tests including hematology, chemistry and liver functions, CT of the abdomen and pelvis, and chest x-ray if indicated. Women of child-bearing potential will have a serum pregnancy test. A laboratory sample (4.5 ml of blood) will also be drawn for patients participating in the 60201 sub-study.

For patients enrolled in Arm A (5-FU, Leucovorin) all laboratory tests will be performed weekly for each cycle of 5-FU and Leucovorin (cycles 1, 3 and 4) and weekly during RT (cycle 2). For patients enrolled in Arm B (EPC, 5-FU) all laboratory tests will be performed weekly during radiation therapy and weekly during chemotherapy cycles. Patients will also be followed during treatment with physical exam at the beginning of each cycle, including vital signs, weight, and toxicity assessment. After treatment is completed, physical exam including vital signs, weight and laboratory tests will be repeated every 3 months for 2 years, every 4 months for 2 years, then yearly for 3 years (7 years total). Disease progression will be assessed by chest x-ray as indicated, at week 30 then yearly for 5 years, and at time of initial tumor progression.

Patients will be provided with nutritional counseling, and monitored for weight loss throughout the treatment portion of the study. Weight loss of > 5% of pretreatment weight will trigger mandatory intervention such as oral supplements, nasal-intestinal feeding tubes, jejunostomy and intravenous alimentation depending on the needs of the patient.

**Progress:** This protocol received initial IRB approval, 26 Apr 05, but was administratively terminated by the IRB prior to final approval in October 2005, for failure to comply with IRB stipulations.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202043	<b>Status:</b> Ongoing
<b>Title:</b> CTSU RTOG 98-04: Phase III Trial of Observation +/- Tamoxifen vs. RT +/- Tamoxifen for Good Risk Duct Carcinoma In-Situ (DCIS) of the Female Breast		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 2/26/2002 - Feb 2005	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** (1) Comparing whole breast radiation +/- Tamoxifen compared to wide excision to negative margins alone +/- Tamoxifen, in decreasing or delaying the appearance of local failure, both invasive and in situ, and preventing need for mastectomy, (2) assess distant disease free survival patients in either arm who fail with progression can be successfully salvaged with further definitive local therapy and adjuvant systemic therapy, (3) setting up a working pathology classification system for DECIS, (4) establishing an epidemiological questionnaire registry for companion studies of biomarkers, and (5) establish tissue bank of patients who progress to local failure in study breast.

**Technical Approach:** To compare the efficacy of Tamoxifen with or without whole breast radiation, in decreasing or delaying the appearance of local failure, both invasive and in-situ, and preventing the need for mastectomy in women with ductal carcinoma in-situ (DCIS) of the breast.

**Progress:** This protocol remains open to patient entry, with no patients enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206112	<b>Status:</b> Ongoing
<b>Title:</b> CTSU/GOG 0218 A Phase III Trial of Carboplatin and Paclitaxel Plus Placebo Versus Carboplatin and Paclitaxel Plus Concurrent Bevacizumab (NSC #704865, IND #7921) Followed By Placebo, Versus Carboplatin and Paclitaxel Plus Concurrent and Extended Bevacizumab, In Women With Newly Diagnosed, Previously Untreated, Suboptimal Advanced Stage Epithelial Ovarian and Primary Peritoneal Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC Louis A. Dainty, MC		
<b>Start - Completion:</b> 11/2/2006 - Sep 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objectives: Determine if the addition of 5 concurrent cycles of Bevacizumab to 6 cycles of standard treatment (carboplatin and paclitaxel) [Arm II] reduces the death rate when compared to 6 cycles of standard treatment alone [Arm I] in women with newly diagnosed suboptimal advanced epithelial ovarian and peritoneal primary cancer; determine if the addition of 5 concurrent cycles plus extended Bevacizumab for 15 months total treatment time to 6 cycles of standard therapy (carboplatin and paclitaxel) [Arm III] reduces the death rate when compared to 6 cycles of standard therapy [Arm I] in this subset of patients.

Secondary objectives: Determine, in the event that both Arm II and Arm III regimens are superior to the Arm I regimen with respect to overall survival, whether the Arm III regimen reduces the death rate when compared to the Arm II regimen; determine whether the Arm II or Arm III regimen increases the duration of progression-free survival when compared with the Arm I regimen; compare each of the experimental regimens to the Arm I regimen with respect to the incidence of severe side effects or serious adverse events; determine the impact on quality of life following treatment with the above regimens; assess the relationship between angiogenic markers and clinical outcome (tumor response, progression-free survival, overall survival) in each of the Arms; assess the predictive value of a set of genes whose expression correlates with survival in these patients.

**Technical Approach:** This is a Phase III study of standard chemotherapy (carboplatin plus paclitaxel) versus standard plus concurrent bevacizumab versus standard plus extended bevacizumab in women with first line, advanced stage epithelial ovarian and primary peritoneal cancer. Patients with a histological diagnosis of FIGO Stage III or IV epithelial or peritoneal primary cancer, with suboptimal residual disease following initial surgery will be screened for enrollment. Patients who qualify will be enrolled and randomized in a 1:1:1 ratio to Arm I, II or III. Randomization will be stratified by stage of disease (Stages III versus IV) and by performance status (0 versus 1 or 2). All patients will receive standard chemotherapy, paclitaxel 175 mg/m<sup>2</sup> IV over 3 hours followed by carboplatin AUC 6 IV over 30 minutes on Day 1 of a 21 day cycle, over 6 cycles. Dose adjustments will be made per protocol for changes in creatinine clearance and for toxicities. Patients in Arm I will also receive placebo on Day1 of Cycle 2 through 6, the placebo every 21 days for an additional 15 months. Patients on Arm II will receive bevacizumab on Day 1 of Cycle 2 through 6, and placebo every 21 days for an additional 15 months. Patients on Arm III will receive bevacizumab on Day 1 of Cycle 2 through 6, and bevacizumab every 21 days for an additional 15 months. Bevacizumab will be given, 15 mg/mg, IV, per package insert. During initial chemotherapy, patients will be assessed at the start of each cycle by physical exam, laboratory tests including CBC, chemistry, LFTs, and CA-125. Patients on anticoagulant therapy will have a repeat PT, PTT and INR prior to each cycle. Blood pressure will be monitored at least weekly

during the first cycle, then prior to each cycle afterwards. Radiographic measurements will be repeated prior to every other cycle. During bevacizumab/placebo treatment these same assessments will be done every other cycle. Post treatment, patients will be followed every 3 months for 2 years, every 6 months for three years, then annually.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 25 July 2006. CIRO approval was obtained 2 November 2006.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206054	<b>Status:</b> Ongoing
<b>Title:</b> NSABP B-38 A Phase III Adjuvant Trial Comparing Three Chemotherapy Regimens in Women with Node-Positive Breast Cancer: Docetaxel/Doxorubicin/Cyclophosphamide (TAC); Dose-Dense (DD) Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel (DD AC-P); DD Doxorubicin/Cyclophosphamide Followed by DD Paclitaxel Plus Gemcitabine (DD AC-PG)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 4/12/2006 - Feb 2011	<b>Funding:</b> CTSU	<b>Periodic Review:</b> N/A

**Study Objective:** The primary aims of this study are to determine whether the DD AC/PG regimen is superior to the TAC regimen as well as to the DD AC/P regimen in improving disease-free survival and to compare the relative disease-free survival of TAC and DD AC/P. Secondary aims are to determine whether DD AC/PG is superior to TAC as well as to DD AC/P in improving overall survival, recurrence-free interval, and distant recurrence-free interval; to compare overall survival, recurrence-free interval, and distant recurrence-free interval of the TAC and DD AC/P regimens, and to compare the relative toxicities of the three regimens.

**Technical Approach:** This Phase III adjuvant therapy trial for women with node-positive breast cancer will compare three regimens of chemotherapy: (1) TAC: docetaxel, doxorubicin, and cyclophosphamide every 3 weeks for 6 cycles, (2) DD AC/P: doxorubicin/cyclophosphamide every 2 weeks for 4 cycles followed by paclitaxel every 2 weeks for 4 cycles (3) DD AC/PG: doxorubicin/cyclophosphamide every 2 weeks for 4 cycles followed by paclitaxel plus gemcitabine every 2 weeks for 4 cycles. Women with operable, invasive carcinoma of the breast with histologically positive axillary nodes will be enrolled and stratified by number of positive nodes, hormone receptor status, and type of surgery and planned radiotherapy. Following stratification, patients will be randomized to one of the three chemotherapy regimens. Women with ER positive and/or PgR-positive tumors should receive hormonal therapy for a minimum of 5 years following completion of chemotherapy. All women who have had a lumpectomy will have radiation therapy. Chest wall and regional nodal irradiation will be prospectively determined at the discretion of the investigator and will be used as a stratification factor. For patients who agree to specimen banking, index tumor blocks as well as tumor blocks collected after diagnosis of contralateral breast cancer will be submitted. Serum will be collected at baseline, at the time of first locoregional or distant recurrence, and when a contralateral breast cancer develops prior to locoregional or distant recurrence. If the first recurrence is an ipsilateral breast tumor recurrence, a serum sample will also be collected at the time of the first subsequent regional or distant recurrence. The study will enroll 4800 patients over a period of approximately 4 years. It is anticipated that the definitive analysis will be carried out approximately 7 years after study initiation.

**Progress:** This protocol remains open to patient entry, with one patient enrolled during FY06. Multiple external adverse events have been reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206073	<b>Status:</b> Ongoing
<b>Title:</b> Phase 1/2 study of ZK-Epothilone (ZK-Epo; ZK 219477) in combination with carboplatin in patients with platinum-sensitive, recurrent ovarian cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 7/11/2006 - May 2010	<b>Funding:</b> Berlex Laboratories via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objective: to establish a dose of ZK-Epo to be used in combination with carboplatin in the subsequent Part 2 of the study. Secondary objective: to investigate the pharmacokinetics of ZK-Epo and carboplatin when given as a combination. Part 2: Primary objective: to investigate the efficacy of ZK-Epo in combination with carboplatin in patients with platinum-sensitive, recurrent ovarian cancer in progression following a first regimen of chemotherapy. Secondary objective: to investigate the safety and tolerability of ZK-Epo in combination with carboplatin in this patient population.

**Technical Approach:** This is a Phase I / II, open label study of ZK-Epothilone (ZK 219477) in combination with carboplatin in patients with platinum sensitive, recurrent ovarian cancer. Patients will be eligible who have progressed after having had one prior chemotherapy regimen including a platinum compound, and who have had a response lasting between 6 and 24 months. Phase I of the study will enroll up to 18 patients in cohorts of 6. Patients will initially be treated at 12 mg/m<sup>2</sup>. Depending on the observed Dose Limiting Toxicities (DLT) the dose will either be decreased to 9 mg/m<sup>2</sup> or increased to 15 mg/m<sup>2</sup>. Patients who develop a DLT will be withdrawn from the study. Patients in Phase I will be required to participate in a pharmacokinetic study to examine the metabolism of ZK-Epo in combination with carboplatin. Patients may also participate in an optional pharmacogenetic substudy. Patients who participate in Part I who appears to benefit from treatment can continue to receive additional cycles of ZK-Epo at the dose level at which they started treatment. Phase II of the study will use the treatment dose determined in Phase I. Up to 30 patients will be enrolled, for a total of 32 evaluable patients. Patients in both phases will be scheduled to receive 2 to 6 cycles of treatment. ZK-Epo will be given per dose escalation, as a 3-hour IV infusion, on Day 1 of a 21 day cycle. Carboplatin will be given at an AUC of 5, as a 30 minute infusion, after ZK-Epo. Patients will sign an approved consent form prior to any study-related procedures. Initial evaluation will include physical exam and history, review in inclusion criteria, disease assessment by CT, MRI or CA-125 level, EKG, and laboratory tests including CBC, chemistry and LFT's. PE and labs will be repeated for each cycles, disease assessment will be repeated every other cycle. Patients will continue treatment until they have received 6 cycles, progress, or are unable to tolerate treatment. After treatment patients will be followed until disease progression. Pharmacokinetic studies will be done for all patients on Phase I, and is option for patients on Phase II. This will consist of thirteen 2.7ml samples drawn within the first 12 hours, and one sample on days 2, 3, 4, 5, 8 and 15. PK samples will only be drawn for the first two cycles of a patient's treatment. Additional pharmacogenetic studies are optional for all patients, and consist of a single blood sample drawn prior to initiation of therapy.

**Progress:** This protocol is open to patient entry, but patient enrollment has not been initiated pending the outcome of discussions with the study sponsor concerning the cost language in the MAMC informed consent document.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204008	<b>Status:</b> Ongoing
<b>Title:</b> Phase II Trial of ONTAK® in Refractory or Relapsed Advanced Non-small Cell Lung Cancer (NSCLC)		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 1/8/2004 - Nov 2005	<b>Funding:</b> Ligand Pharmaceuticals, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 10/19/2006

**Study Objective:** (1) To evaluate the safety of ONTAK® (denileukin diftitox, DAB389IL-2) in patients with NSCLC, (2) To evaluate the efficacy of ONTAK® in patients with NSCLC. (3) To evaluate the value of soluble Interleukin-2 receptors (IL2R) in predicting tumor response (or reaction) to ONTAK®. (4) To evaluate the correlation between tumor IL2R status and disease response to treatment.

**Technical Approach:** This is a Phase II multicenter non-randomized open label clinical trial. Up to 50 subjects will be enrolled in the overall study with a goal of having 42 evaluable subjects. At MAMC, 2-4 subjects may be enrolled from subjects receiving treatment for lung cancer in the Hematology and Oncology Clinic. Treatment will consist of IV administration of ONTAK® daily for 5 days every 3 weeks. Safety assessments will include laboratory hematology and blood chemistry tests, physical exam and vital signs, and ECOG status and toxicity assessments.

During the first cycle of treatment, toxicities will be evaluated weekly using the NCI Common Toxicity Criteria, then each cycle afterwards. Serious Adverse Events will be reported to the IRB, FDA, and to the study drug manufacturer. Tumor response will be assessed by physical exam, CT scan, and other appropriate imaging studies performed every 2 cycles and evaluated using the RECIST criteria. Subjects with tumor response or stable disease will receive up to 6 cycles of study treatment. Subjects with progressive disease or unacceptable toxicity will be removed from the study. Interim evaluation is planned after the first 14 evaluable subjects. If no subjects experience an objective response or stable disease, then the study will be terminated. Soluble IL2 receptor (IL2R) levels in serum will be measured to study the value in predicting tumor reaction or response to the treatment, and evaluation of tumor IL2R status and CD 25 staining will be performed by the central study site laboratory. Primary efficacy endpoints are the response rate, overall survival, and time to disease progression. Primary safety endpoints are the number of cycles of therapy administered and the type and grade of toxicities. Secondary endpoints will be the level of soluble IL-2 receptor in serum and receptor expression in the tumor tissue (positive or negative).

**Progress:** This protocol closed to enrollment with two subjects enrolled. One subject is deceased and the other subject continued to be followed during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206084	<b>Status:</b> Ongoing
<b>Title:</b> Pilot Study to Evaluate the Safety and Efficacy of PROCRIT (Epoetin alfa) 80,000 Units Once Every Four Weeks (Q4W) vs. 40,000 Units Once Every Two Weeks (Q2W) in Cancer Patients with Non-Chemotherapy Anemia		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 7/12/2006 - Dec 2009	<b>Funding:</b> Henry M. Jackson via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Objectives: To investigate the safety and efficacy of PROCRIT 80,000 units (U) once every 4 weeks and 40,000U once every 2 weeks subcutaneously in anemic subjects with cancer not receiving chemotherapy or radiation therapy and to assess the effects of the dosing regimens on time-to- hematopoietic-response, and transfusion requirements.

**Technical Approach:** This is a prospective, randomized, open-label, multi-center pilot study to evaluate the safety and efficacy of PROCRIT (Epoetin alfa) 80,000 Units once every four weeks versus 40,000 Units (U) once every two weeks in cancer patients with non-chemotherapy anemia. A total of 100 subjects will be enrolled and up to 10 at MAMC. Patients with confirmed non-myeloid malignancy, who are anemic, and not receiving chemotherapy or radiation will be randomized in to one of two treatment groups receiving Procrit. Safety data that will be obtained during the study includes height, weight, blood tests, blood pressure and incidence and severity of adverse events. Patients will be randomized to one of two treatments groups receiving PROCRIT subcutaneously. The starting dose will be either 80,000 U every 4 weeks with a maximum treatment period of 13 weeks or 40,000 U every 2 weeks with a maximum period of 15 weeks. A follow-up visit will occur for both treatment groups on weeks 17. Hemoglobin levels will be obtained every week to monitor hemoglobin rate of rise for safety. The target hemoglobin is 10 to 12 g/dL. Patient will be screened for study eligibility at the screening visit occurring up to 14 days prior to treatment with study drug unless otherwise specified. They will be followed up to week 17. An interim analysis will be performed when the first 40 enrolled subjects have completed or withdrew from the study. The primary efficacy end point will be hematopoietic response, defined as < 1 g/dL rise in hemoglobin.

**Progress:** This protocol remains open to patient entry, with no patients enrolled.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204080	<b>Status:</b> Ongoing
<b>Title:</b> Protocol U2963n: The National Lymphocare Study: An Observational Study of Treatment, Outcomes, and Prognosis in Patients With Follicular Non-Hodgkin's Lymphoma		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwicz, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 8/16/2004 - Aug 2014	<b>Funding:</b> Genentech via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** The objective of this study is to delineate differences in treatment outcome for patients with follicular non-Hodgkin's lymphoma (NHL) by comparing the outcomes and safety of common front-line and subsequent therapeutic strategies. The planned comparisons address clinical questions including the role of watchful waiting, use of anthracyclines in front-line therapy, and role of maintenance therapy, and treatment sequencing. Reported outcomes for a given treatment strategy will include a description of these outcomes based on Follicular Lymphoma International Prognostic Index (FLIPI) score risk stratification at the time of diagnosis and subsequent treatment initiation.

**Technical Approach:** This is a prospective, observational, longitudinal, multicenter study of patients with newly diagnosed follicular Non-Hodgkin's Lymphoma (NHL). 12-18 patients may be enrolled at MAMC, and approximately 5000 patients in the United States. A database will be created containing patient and tumor characteristics and treatment and outcome information. All patients at participating sites diagnosed with follicular NHL within 6 months prior to enrollment will be eligible, regardless of specific treatments received (including investigational products) and including patients followed using a watch-and-wait approach. Patients will receive treatment and evaluations for NHL according to the treating physician's standard of care and clinical practice. No study-specific visits, interventions or patient evaluations will be conducted. Patient data will be collected from medical records and reported by means of a Web-based Electronic Data Collection System (EDC). All treatments patients receive for NHL will be recorded and treatment outcomes will be collected quarterly. Enrolled patients will be followed for up to 10 years or until death, withdrawal of consent, loss to follow up, or study termination. Study feasibility reviews will be conducted at 2, 5, 7, and 10 years. Outcome measures include: time from initial diagnosis to initial therapy; time from initial therapy to subsequent therapy, response to treatment (initial and subsequent) as assessed by the treating physician; time to disease progression; survival time; lymphoma treatment-related toxicity as measured by death, early treatment discontinuation, and hospitalization; and FLIPI score. This is an observational cohort study and is not designed to evaluate a predefined hypothesis. However, effectiveness and safety outcomes will be analyzed, confidence intervals for differences will be reported, and standard statistical tests will be performed, with the first evaluation taking place after approximately 500 patients have been enrolled for at least 6 months.

**Progress:** This protocol remains open to enrollment with four subjects consented. One subject has died and three continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202107	<b>Status:</b> Completed
<b>Title:</b> Randomized Study of Docetaxel Versus Docetaxel Plus Genasense™ (G3139; Bcl-2 Antisense Oligonucleotide) in Patients with Previously Treated Non-Small Cell Lung Cancer, No. N304		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 9/30/2002 - Sep 2004	<b>Funding:</b> Genta Inc via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** (1) To compare the survival of subjects with advanced non-small cell lung cancer treated with docetaxel alone versus docetaxel combined with Genasense (Bcl-2 antisense oligonucleotide). (2) To compare response, time to progression, tumor-related symptoms, and safety in the two treatment groups.

**Technical Approach:** In this advanced non-small cell lung cancer study antisense treatment will be given with Taxotere (docetaxel) and tumor response and safety will be compared to therapy with Taxotere alone. This study is a randomized, multicenter, open label, Phase III design clinical trial. This Phase III study will include a minimum of 280 patients randomized in a 1:1 ratio to Docetaxel or Docetaxel + Genasense. Approximately 35 centers will participate. Study endpoints include the primary efficacy variable of survival and secondary efficacy variables of response rate, proportion of patients surviving at 6 and 12 months, duration of response, time to disease progression and other measures of clinical benefit such as change in performance status. All patients in the study will be prospectively stratified by response to prior chemotherapy regimen, ECOG performance status and prior paclitaxel treatment.

**Progress:** This protocol closed to enrollment in July 2004, when accrual goals were met. Three subjects enrolled at MAMC; all were reported deceased by July 2005, due to disease progression. A site close out visit was reported in September 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206055	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0424: Molecular Epidemiology Case-Series Study of Non-Small Cell Lung Cancer in Smoking and Non-Smoking Women and Men		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 8/3/2006 - Feb 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To assess lung tissue from cancer patients for specific tobacco smoke carcinogens, alterations in specific genes, and to determine whether these factors differ by gender and smoking status, adjusting for potential exposures and influential factors including family smoking status, medication use, hormonal and reproductive factors. To measure levels of (PAH)-DNA adducts in tissues and see if levels are higher in females than males for the same level of smoking.

**Technical Approach:** Eligible patients would be asked to complete a questionnaire about smoking, reproductive history, occupational exposures and other factors. Samples of cancer tissue obtained at the time of biopsy or operation would be sent to a special laboratory to study genetic changes that may explain why women are more susceptible to tobacco smoke chemicals. A blood specimen would be sent to a special laboratory for scientific testing to help learn more about the causes of lung cancer and who is at risk to identify who would benefit from intensive screening and possible interventions. The results of the testing will not be released to the patient or study physician.

**Progress:** This protocol is open to patient entry, with no patients enrolled during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206013	<b>Status:</b> Ongoing
<b>Title:</b> SWOG S0435 A Phase II Trial of BAY 43-9006 (SNC-724772) in Patients with Platinum-Treated Extensive Stage Small Cell Lung Cancer		
<b>Principal Investigator:</b> LTC David E. McCune, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC		
<b>Start - Completion:</b> 1/18/2006 - Nov 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 11/21/2006

**Study Objective:** Primary endpoints: to evaluate the efficacy of BAY 43-9006 in previously-treated, platinum-sensitive and platinum-refractory patients with measurable disease and extensive stage small cell lung cancer (E-SCLC) in terms of response rate (confirmed and unconfirmed, complete and partial). Secondary endpoints: to assess the qualitative and quantitative toxicities of BAY 43-9006 in this patient population. To assess overall survival in this group of patients treated with BAY 43-9006. To collect specimens via the Lung Cancer Specimen Repository Protocol (S9925) in order to perform exploratory analyses of the relationship between selected markers and patient outcomes.

**Technical Approach:** This is a Phase II, multi-center trial of BAY 43-9006 in patients with platinum-treated extensive stage small cell lung cancer. BAY-43-9006, or Sorafenib, is a compound that inhibits multiple tyrosine kinase pathways involved in tumor progression. Patients will be enrolled who have had prior treatment with platinum based therapy. Accrual will proceed separately in two strata based on whether patients are platinum sensitive or resistant. Patients will undergo screening, with medical history and physical, head and chest CT scans, bone scan if indicated, and blood tests for chemistry and CBC. Patients will also be offered participation in S9925, a companion study for specimen submission. Eligible patients will be treated with an oral dose of BAY 43-9006, 400mg twice a day in a 4 week cycle until disease progression. Ongoing assessments will include weekly toxicity assessment, CBC every other week, and physical exam chemistry every 4 weeks. Disease assessment will include scans every 8 weeks during treatment, and every 3 months after treatment for up to 2 years after enrollment, or until death. Enrollment will continue until 20 each of platinum sensitive and platinum resistant patients have been enrolled, after which an additional 20 patients will be enrolled to each group if there has been at least one response to treatment.

**Progress:** This protocol remains open to patient entry to the platinum refractory arm of the study. One patient enrolled during FY06, but died of progressive disease after declining further treatment due to serious adverse events of gait instability, slurred speech and confusion.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205036	<b>Status:</b> Ongoing
<b>Title:</b> CTSU NSABP C-08, A Phase III Clinical Trial Comparing Infusional 5-Fluorouracil (5-FU), Leucovorin, And Oxaliplatin (mFOLFOX6) Every Two Weeks With Bevacizumab To The Same Regimen Without Bevacizumab For The Treatment Of Patients With Resected Stages II And III Carcinoma of the Colon		
<b>Principal Investigator:</b> MAJ Angela G. Mysliwiec, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC David E. McCune, MC; MAJ Jasmine T. Daniels, MC		
<b>Start - Completion:</b> 5/3/2005 - Mar 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006
<p><b>Study Objective:</b> Primary Objective is to compare the relative efficacy of mFOLFOX6 + bevacizumab with that of mFOLFOX6 alone in prolonging disease-free survival (DFS). Secondary Objective is to compare the relative efficacy of mFOLFOX6 + bevacizumab with that of mFOLFOX6 alone in prolonging survival (S).</p> <p><b>Technical Approach:</b> Eligible subjects will be randomized into one of the two study groups. Patients in Group 1 will receive the drugs 5-FU, Leucovorin, and Oxaliplatin, repeated every 14 days (one cycle) for a total of 12 cycles of chemotherapy. Patients in Group 2 will receive 5-FU, Leucovorin, and Oxaliplatin, repeated every 14 days (one cycle) for a total of 12 cycles of chemotherapy and also receive bevacizumab on day 1 of each cycle before receiving the chemotherapy. After chemotherapy is done, subjects will continue to receive bevacizumab once every 2 weeks for another 6 months. Subjects will continue to be followed for the first 5 years with physical exams, urine and blood tests, and an enema with x-ray or endoscopic exam. National accrual is expected to be 2632 patients over 4 years. Investigators estimate approximately 4 patients per year for a total of 16 patients enrolled at MAMC.</p> <p><b>Progress:</b> This study closed to enrollment 6 October 2006 after NSABP enrollment goals were met. Four patients enrolled at MAMC and remained in treatment or follow-up during FY06.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206025	<b>Status:</b> Terminated
<b>Title:</b> RegistHER: An Observational Cohort Study of Patients with HER2-Positive Metastatic Breast Cancer		
<b>Principal Investigator:</b> MAJ Angela G. Mysliwiec, MC		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 12/14/2005 - Jan 2011	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objectives are to describe the time to treatment failure, time to disease progression, overall survival, incidence of clinically significant cardiac-related adverse events in a cohort of patients with HER2-positive metastatic breast cancer and to describe and compare the outcomes associated with common therapies.

**Technical Approach:** This is a prospective observational cohort study designed to describe the effectiveness and safety (treatment outcomes and clinically significant cardiac adverse events) in patients with HER2-positive metastatic breast cancer. Enrolled patients will receive treatment and evaluations for HER2-positive metastatic breast cancer as determined by their treating physicians according to the standard of care and clinical judgement. The study will enroll > 1000 patients over approximately 2-3 years. Patients will be followed from enrollment until death, withdrawal of consent, or loss to follow-up.

**Progress:** This protocol was terminated 2 March 2006, due to failed contract negotiations with the study sponsor. The study was never initiated at MAMC.

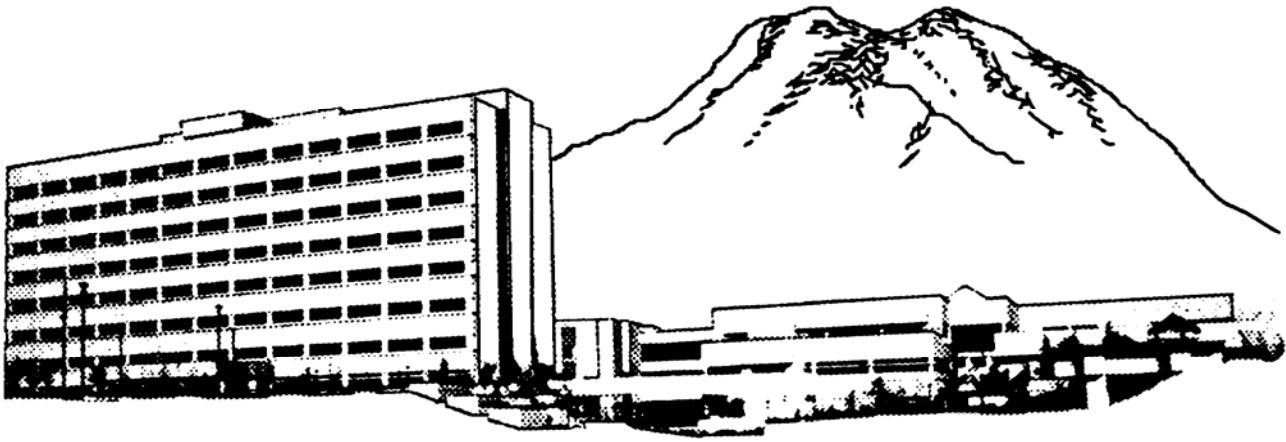
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204082	<b>Status:</b> Ongoing
<b>Title:</b> Evaluating Cognitive Function in Women Receiving Chemotherapy for Newly Diagnosed Breast Cancer		
<b>Principal Investigator:</b> Margaret J. Ramsdell, RN, BSN, OCN		
<b>Department:</b> Medicine/Hematology & Oncology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Donna L. Berry, Ph.D., RN		
<b>Start - Completion:</b> 5/25/2004 - Oct 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** To evaluate cognitive function in women newly diagnosed with breast cancer, receiving chemotherapy and the effect of cognitive function on the individual's quality of life. This study will examine both the relationship between cognitive function scores and patient's self-reported cognitive problems and the meaning of the measures for women receiving chemotherapy for breast cancer. Specifically: (1) to describe function scores of the EORTC QLQ C-30 cognitive subscale and the High Sensitivity Cognitive Screen (HSCS) in women with breast cancer at baseline and mid point in chemotherapy treatment for breast cancer, and (2) to evaluate the process and meaning of answers on the HSCS and the cognitive subscale questions of the EORTC QLQ C-30 questionnaire.

**Technical Approach:** This study will utilize a longitudinal, pre-post test design to evaluate women newly diagnosed with breast cancer who will be receiving doxorubicin and cyclophosphamide. Women ages 25-70, newly diagnosed with breast cancer will be asked to participate in this study. Subjects interested will fill out a 3x5 card with name and phone number and will be contacted by the PI. After signing consent and answering questions, patients will fill out the EORTC QLQ C-30 questionnaire. Upon completion of the EORTC QLQ C-30 a cognitive interview of those questions will be conducted to find out how the subjects felt about reading and answering the questions, what those questions mean to them and how their cognitive function currently is affecting their quality of life. The HSCS, a sensitive tool for detecting subtle cognitive impairment, will be administered at the completion of the cognitive interview. Descriptive statistics will be used to summarize the demographic characteristics of the EORTC QLQ C-30 cognitive scale scores and the cognitive domain scores on the HSCS of the subjects of two time points per chemotherapy and at mid point during chemotherapy. The Mann-Whitney test will be used to compare cognitive scale scores on the EORTC QLQ C-30 and cognitive domain scores on the HSCS in subjects at the same time point. The results at both time points will be graded and examined for changes in scores on the HSCS as well as changes in the five item subscale of the EORTC QLQ C-30 .

**Progress:** This protocol closed to enrollment in May 2006, with 6 subjects enrolled. Data collection is complete and the study remains ongoing to complete data analysis and the final manuscript.



## **Detail Summary Sheets**

Internal Medicine Service, Department of  
Medicine



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205046	<b>Status:</b> Ongoing
<b>Title:</b> The Effect of Blood Transfusion on Serum Ferritin and Iron		
<b>Principal Investigator:</b> CPT Corinna Avalos, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Ashley A. Feaver, MC; LTC Rajat Bannerji, MC; CPT Daniel G. Cuadrado, MC; COL Ronald H. Cooper, MC; CPT Patrick M. McNutt, MS		
<b>Start - Completion:</b> 5/26/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** To study the effect of packed red blood cell transfusion on ferritin level and iron panel.

**Technical Approach:** In this descriptive study a database containing demographic and medical information will be constructed for patients who have anemia requiring non-emergent packed red blood cell transfusions. Candidates for the study will be identified by a list of excluding medical conditions a physician will go through prior to the transfusion and consent. Eligible patients who consent to the study will have their iron panel and ferritin levels drawn prior to transfusion and six other times as specified after transfusion.

**Progress:** This protocol remains ongoing at MAMC, with four out of five subjects completing the required lab work. One subject died prior to completing the lab work; this death was unrelated to study participation. Due to time constraints, enrollment has been on hold, but investigators plan to resume enrollment during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205123	<b>Status:</b> Ongoing
<b>Title:</b> Current Use and Complications of Peripherally Inserted Central Catheters (PICC): A Retrospective Study		
<b>Principal Investigator:</b> CPT Kathleen C. Bauler, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Joel T. Abbott, MC; MAJ Alexander S. Niven, MC; MAJ Cecily K. Peterson, MC		
<b>Start - Completion:</b> 8/18/2005 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** Evaluate the indications for placement, duration of therapy and complications of peripherally inserted central catheters (PICC) lines in the inpatient population at Madigan Army Medical Center.

**Technical Approach:** This is a retrospective chart review of consecutive inpatients with PICC lines as identified from PICC service records. Subjects without documentation of a minimum of one endpoint will be excluded from further analysis and recorded by clinical service as "no data available." A data sheet will be completed for subjects with a minimum of one recorded end point (PICC line placement, removal or "unknown" re: PICC). Each subject's demographics, pertinent medical history, indication, duration, and complications of PICC line placement, nurse placing PICC line and years of experience will be recorded. 100 consecutive subject's charts will be reviewed using this criterion. Primary variables will be indication, duration of therapy, and complications. Subjects with and without complications will be separated and analyzed by indication, duration of therapy, demographic and medical information, and nursing information. Data will be analyzed using Chi-squared, ANOVA and MANOVA analysis.

**Progress:** This retrospective review protocol continues to collect patient information. Several patient charts selected were found not to have had PICC lines placed; rather patients had other central lines placed. The PI has discussed other means of collecting data on patients with PICC lines. At this time, 25 patients out of nearly 70 reviewed have been eligible for analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205039	<b>Status:</b> Ongoing
<b>Title:</b> Management of Parapneumonic Effusions: Does Following Pneumonia Treatment Guidelines Affect Outcome? A Retrospective Study		
<b>Principal Investigator:</b> CPT Patricia J. Dehaan, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Bernard J. Roth, MC; John G. Meyer, MD; MAJ John P. Rinard, MC		
<b>Start - Completion:</b> 2/11/2005 - Aug 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/12/2006

**Study Objective:** To determine whether pneumonia treatment guidelines are being followed at Madigan Army Medical Center in managing parapneumonic effusion and whether outcome is affected via retrospective chart review.

**Technical Approach:** This is a retrospective study of parapneumonic effusions in patients with the diagnosis of community-acquired pneumonia (CAP). Adult patients (age 18 years and older) that meet the diagnosis of pneumonia will be studied to determine whether a parapneumonic effusion (PPE) was present at time of diagnosis and if pneumonia management guidelines published by the IDSA and ATS were followed. If a PPE was present on chest radiograph, was a lateral decubitus study or CT scan then done? If the PPE layered >10 mm on lateral decubitus radiograph, was thoracentesis done? Did it change patient management and was outcome affected? If no difference of outcome is found, should the pneumonia management guidelines be updated? This study will look at patients given the diagnosis of CAP during the time frame from 01 Jan 02 to 31 Dec 03.

**Progress:** This protocol remains ongoing. Data collection is complete but investigators are compiling the findings for publication in a medical journal.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206119	<b>Status:</b> Ongoing
<b>Title:</b> Urinary Markers of Renal Injury and N-Acetylcysteine Efficacy (URINE)		
<b>Principal Investigator:</b> CPT Nathan R. Evans, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Howard M. Cushner, MC; MAJ Jason L. Davis, MC; CPT Mehdi C. Shelhamer, MC		
<b>Start - Completion:</b> 10/18/2006 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to attempt to measure NAC's effect at the renal tubular cell level by measuring two known markers for renal cell injury after a contrast load. A secondary objective will be to look into differences in these urinary enzyme levels based on how much IV contrast volume was given in both the study and control groups.

**Technical Approach:** Up to 90 patients who have been scheduled for a radiologic imaging study with IV contrast or heart catheterization will be recruited for this study. An additional 45 patients scheduled for a non-invasive imaging study such as an ultrasound will also be recruited. The goal is to enroll 135 patients who complete the study. Patients will be stratified by age (<50 and >50) and creatinine clearance (60-90 versus >90) as calculated by the MDRD equation<sup>20</sup> using a completed chem 7 or 14. The patients undergoing a heart catheterization or IV radiologic imaging study will be randomized to either NAC or no NAC using a computer program based on random number generation. NAC will be administered in 4 ounces of orange juice and control patients will receive an equivalent volume of normal saline (as NAC), also in 4 ounces of orange juice. Patients will be blinded to treatment and questioned as to which treatment they believe they received after the first dose and at the end of the study. 45 patients will be enrolled in a study group receiving NAC prophylaxis for their contrast study. 45 patients will serve in a control group, which will not receive NAC. The study will remain open until 45 patients are enrolled in each group. GGT and NAG will be measured from urine collections prior to the administration of NAC and contrast and 24 hours after the administration of contrast. A 50 cc spot urine specimen will be collected on all patients prior to taking the first dose of NAC. A second 50 cc spot urine specimen will then be collected 24 hours after the contrast study. Both urine specimens will be used to measure urine GGT and NAG levels standardized per gram of urine creatinine. The age, race, sex, baseline MDRD GFR, presence of diabetes, use of ACE inhibitor and amount of IV contrast volume given to each patient will also be recorded. Only the IND pharmacist will be aware of whether NAC is given to the patient (via computer generated randomization). Patients and investigators will be blinded as to who will receive NAC.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 22 August 2006. Final approval was granted 18 October 2006.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206064	<b>Status:</b> Completed
<b>Title:</b> Does Participation in a Subspecialty Elective Rotation Improve the Respective American Board of Internal Medicine Subspecialty Score?		
<b>Principal Investigator:</b> CPT Collin J. Fischer, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Cecily K. Peterson, MC; CPT James A. Watts, MC		
<b>Start - Completion:</b> 3/6/2006 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To determine if internal medicine resident participation in a one month internal medicine subspecialty elective significantly affects the score of that particular subspecialty on the American Board of Internal Medicine (ABIM) Certification Examination. (2) To determine if internal medicine resident participation in all eight core internal medicine subspecialty elective rotations (i.e. cardiology, pulmonary medicine, gastroenterology, nephrology, infectious disease, rheumatology, hematology/oncology and endocrinology) confers a benefit as measured by the overall ABIM Certification Examination score when compared to residents who did not participate in all eight core internal medicine subspecialty elective rotations during residency training. (3) To determine if internal medicine resident participation in four months or more of "non medicine" electives during residency training is prognostic of a significantly worse overall score on the ABIM.

**Technical Approach:** The specific subspecialty clinical rotations, ABIM Certifying Examination (ABIMCE) total and subspecialty scores/deciles, and PGY-2 In Training Examination (ITE) total score will be collected for each subject. Information on which subspecialty clinical rotations were completed will be obtained from an examination of clinical evaluation forms completed at the end of each clinical rotation. (1) Participants will be grouped within each subspecialty according to number of months they spent performing that subspecialty elective during their PGY 2 and 3 years (0, 1 and >1 months). Subjects will be paired according to their PGY-2 ITE percentile by year score. ABIM subspecialty scores will be compared for statistically significant differences between groups with the ANOVA test. (2) Subjects will be divided into 2 groups based on completion of the entire set of 8 internal medicine "core electives" (defined above) versus non-completion. Subjects will then be paired according to PGY-2 ITE percentile by year score. Total ABIMCE scores will be compared for statistically significant differences between groups with a 2 tailed Student's t-test. (3) The number of "non-medicine" electives will be tallied for each subject. A "non-medicine" elective will be defined as any elective on which the preponderance of time is spent on a subject not tested on the ABIMCE. Subjects will then be split into groups based on participation in <4 or >4 "non-medicine" elective months during residency, and paired according to their PGY-2 ITE percentile score. Total ABIMCE scores will be compared for statistically significant differences between groups with a 2 tailed Student's t-test.

**Progress:** This protocol was reported completed in July 2006. Results: Mean In-Training Examination scores during the PGY-2 year was 64th percentile. The average ABIMCE overall decile for the group was 7.2. The group had a 97% first time pass rate on the ABIMCE. Overall, performing one or more months on a medicine subspecialty elective did not correlate with higher sub-score for that speciality. In addition, completing the 'core' 8 medicine subspecialty elective rotations during residency did not predict a significantly better overall score on the ABIMCE. However, performing more non-medicine related electives was correlated with a significantly worse overall score on the ABIMCE. The cut-off for this significance is 4 or more non-medicine rounds.

Conclusions: Obtaining ABIM certification is an expected goal of Internal Medicine graduates and residency programs. However, the ABIMCE is only validated to assess the medical knowledge competency. Furthermore, for any individual, subspecialty sub-scores on the ABIMCE are only important when one does not achieve certification on the first attempt. Hence, the factors that drive subspecialty elective choice by residents (or requirements by programs) must include other issues including demonstrating all the core competencies in that subspecialty discipline.

What our data does support is that even in this population skewed toward above average success on the ABIMCE, increased numbers of non-medicine electives correlated with poorer overall performance. At a micro level, this finding may influence program limitation on non-medicine electives in residents at risk for not passing the ABIMCE on the first attempt. At a macro level, this data is important to the academic Internal Medicine community as restructuring residency training is being considered nationally.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205104	<b>Status:</b> Completed
<b>Title:</b> Appropriate Use of CTPA in the Evaluation of Pulmonary Embolism - An Examination of Hospital-Wide Referral Practices		
<b>Principal Investigator:</b> CPT Cristin A. Kiley, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Vincent Mysliwicz, MC; MAJ Kristie J. Lowry, MC		
<b>Start - Completion:</b> 7/12/2005 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to ascertain the physician ordering practices for CT Pulmonary Angiography (CTPA) in the context of diagnosing pulmonary embolism (PE) and to determine if these ordering practices meet accepted community standards.

**Technical Approach:** Patients who fit the initial study population will have their charts reviewed by the investigators who will determine their modified Well's score for probability of pulmonary embolism: i.e., the presence of a d-Dimer assay will be noted along with its result, EKG and CXR findings, symptoms upon presentation, the result of the CTPA and documentation pre-test and post-test will all be reviewed. Based on accepted guidelines, a determination will be made if the study was ordered appropriately. The percentage of CTPAs with positive findings will be calculated and correlated with the number of studies to determine if MAMC ordering practices meet community standards. Both pre and post test documentation concerning follow-up for incidental abnormalities found on CTPA will be examined. If the data gathered suggest that MAMC providers are ordering CTPAs inappropriately compared with community standards, a proposal for initiating referral guidelines for CTPA to rule out PE in the MAMC health care system will be put forth.

**Progress:** This protocol was reported completed in June 2006. Results: Of 394 charts reviewed, 303 patients underwent CTPA imaging and were included in further analysis. A Simplified Wells score was calculated in 279 (92%) subjects, with a mean score of 1.6 + 1.6. 145 subjects had D-dimers performed, of which 128 (88%) were positive. 20 CTPA were positive for VTE, a positive rate of 7.2%. No subjects had a negative D-dimer and a positive CTPA. Follow-up imaging was recommended in 145 (52%) of cases. Conclusion: This study demonstrated a statistically significant lower rate of CTPA positivity. The expected positive rate for MAMC was 16%, the actual rate was 7.2% (p=.0004). Additionally, the sensitivity of the D-dimer was 100% with a specificity of 22%. This is a result of failure to adhere to a validated clinical algorithm to assess for VTE and a large proportion of low clinical probability patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206087	<b>Status:</b> Ongoing
<b>Title:</b> Hemoptysis in Young Adults		
<b>Principal Investigator:</b> CPT Herbert P. Kwon, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Vincent Mysliwicz, MC		
<b>Start - Completion:</b> 5/8/2006 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To report in case series format the causes of hemoptysis in young adults as determined by bronchoscopy at the MAMC Pulmonary clinic in a retrospective medical record review.

**Technical Approach:** A retrospective chart review will be performed utilizing the MAMC Pulmonary Clinic Bronchoscopy logbook as the initial source of patient identification. The logbook for the years of 2000-2006 will be screened for individuals undergoing bronchoscopy within the age range of 18 through 45 years of age. The indication for bronchoscopy will be screened for hemoptysis.

**Progress:** Nineteen subject's records were identified for inclusion in this retrospective review protocol during FY06. The results collected so far will be presented at Army ACP, November 2006 in Washington D.C. The protocol remains ongoing at MAMC.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206069	<b>Status:</b> Ongoing
<b>Title:</b> The Effects of Nighttime Low Dose Aspirin on Ambulatory Blood Pressure Testing in Treated Hypertensive Patients		
<b>Principal Investigator:</b> CPT Herbert P. Kwon, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jason L. Davis, MC		
<b>Start - Completion:</b> 6/12/2006 - Dec 2006	<b>Funding:</b> DCI via Spacelabs	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the benefits of aspirin chronotherapy in patients already on anti-hypertensive therapy.

**Technical Approach:** Eligible patients who consent to participate will have a baseline physical exam performed that will include a cardiovascular exam. If signify underlying occult organic heart disease is detected the patient will not be included in the study. If the work up is negative, the patient will be included in the study. After an evening of fasting, patients will have six blood pressure measurements taken after sitting for at least 5 minutes. All efforts will be made to ensure the measurements are taken on the same type of machine by the same individual, and at the relatively same times in the morning (between 0800 and 1100). Patients will be randomly assigned to either remain on their aspirin in the morning or to take it nightly. Patients will then have physical measurements taken and their fasting blood drawn. Finally, a Spacelabs 90207 Ambulatory Blood Pressure Monitor {ABPM} (Issaquah, Washington) will be placed and instructions for use given.

**Ambulatory Blood Pressure Monitor:** Patients will have blood pressure and heart rates measured every 20 minutes between 0700 and 2300 if they are civilian and 0600 and 2200 if they military participants. During the eight hour "rest period" patients will have measurements taken every 30 minutes. Data will not be used if there is >30% of measurements missing, data missing for more than 2 hours, or if patients fail to return for a second ambulatory blood pressure measurement. After returning the blood pressure monitor, patients will receive a new bottle of aspirin with a sticker stating if the medication should be taken in the morning or evening in addition to the normal written instructions, which will conclude initial randomization to a study arm. Investigators will be blinded to the timing of aspirin administration. Measurements will be submitted via email at Months 0-3 (First Inter-measurement Period), Month 3 (Interim Evaluation) and Months 4-6 (Second Inter-measurement Period. Patients will have the timing of their low dose aspirin reversed, serving as their own controls and cross-overs. Participants who took it in the evening will now take it in the morning and vice versa. Patients will be contacted, encouraged to stay consistent with the protocol, and/or to contact Dr. Kwon or study staff. The values obtained for the ABPM and the fasting labs at the interim evaluation above will be used also for the baseline for the second inter-measurement period.

**Final Evaluation:** After the final three months of therapy patients will return for a fasting laboratory sampling, appointment and re-measurement of blood pressure to include another 48 hour AMBP. Medical records will be reviewed for any interim visits, hospitalizations, or medication changes. Patients will be asked if they suffered any increase in side effects or gastrointestinal discomfort during the study period.

**Progress:** This study was delayed for five months prior to enrolling patients. Three months following initial IRB review, the Department of Nursing made multiple reviews of the study prior to releasing their impact statement in support of this study. It was further delayed for two months

when Clinical Engineering stated that the necessary equipment could not be held or utilized at the hospital for the allotted timeframe of the study. After a lengthy debate and review of the CRADA/SOW, Clinical Engineering approved the equipment for use at MAMC. No subjects enrolled during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205038	<b>Status:</b> Terminated
<b>Title:</b> Effect of A Single Intra-articular Steroid Injection on Serum Fructosamine Levels in Patients with Type 2 Diabetes Mellitus		
<b>Principal Investigator:</b> CPT George R. Mount, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Cristin A. Kiley, MC; MAJ Brian T. McKinley, MC; CPT Kyle C. Harner, MC		
<b>Start - Completion:</b> 2/3/2005 - Jan 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to observe the effect that a single dose of corticosteroid (40mg kenalog, 1cc) injected into the knee joint has on the serum glucose level in individuals with type 2 diabetes mellitus.

**Technical Approach:** Subjects presenting to the Rheumatology clinic for intra-articular steroid injection into the knee, who have Diabetes Mellitus and are not currently taking insulin therapy will be deemed eligible for the study. Subjects who meet the criteria will offered consented. If they do wish to participate, the consent form will be signed and the patient will receive their joint injection. Subjects will report to the lab immediately after joint injection for Fructosamine level and HbA1c. Subjects will return to the lab in two weeks for Fructosamine level. Subjects will return to the lab in two weeks (4 weeks from time of injection) for Fructsamine level and HbA1c. Subject participation will be complete at this time. Lab results will be gathered by the investigators and the data will be analyzed.

**Progress:** This protocol was terminated by investigators in June 2006 due to a lack of accrual.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202048	<b>Status:</b> Ongoing
<b>Title:</b> A Multinational, Randomized, Double-blind, Placebo-controlled, Forced-titration, 2X2 Factorial Design Study of the Efficacy and Safety of Long Term Administration of Nateglinide and Valsartan in the Prevention of Diabetes and Cardiovascular Outcomes in Subjects with Impaired Glucose Tolerance (IGT), Protocol No. CDJN608 B2302		
<b>Principal Investigator:</b> MAJ Patricia A. Short, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jon C. Allison, MC; Marvin Y. Hayami, M.D.; MAJ Cecily K. Peterson, MC; Shaila B. Kode, M.D.		
<b>Start - Completion:</b> 4/19/2002 - Aug 2009	<b>Funding:</b> Novartis via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** Core Phase: to evaluate the effect of long-term administration of nateglinide and valsartan on the progression to diabetes in subjects with impaired glucose tolerance (IGT) at increased risk of a cardiovascular event. Extension Phase: to evaluate the effect of long-term administration of nateglinide and valsartan on cardiovascular morbidity and mortality. Definition of this composite endpoint is provided on page 11 of the attached Protocol, and is further discussed in the Summary to this cover document.

**Technical Approach:** Approximately 24 subjects will be enrolled at MAMC. Study design projects enrollment of 7500 subjects from 600-800 centers in about 40 countries, with approximately 1875 subjects in each of 4 treatment groups. 75% of subjects will receive at least one of the study drugs. All study drugs are taken orally. Patients will be invited to participate in screening who have one or more risk factors for the conditions under study (such as family history, known IGT, high BMI, dyslipidemia.) Eligible patients will be randomized into one of four groups (1. Nateglinide 60 mg before meals + matching placebo once daily; 2. Nateglinide 60mg before meals + Valsartan 160mg once daily; 3. Matching placebo before meals + matching placebo once daily; 4. Matching placebo before meals + Valsartan 160mg once daily) using an electronic interactive voice recognition system. There will be sixteen study visits after initiation of study treatment: at +2 weeks, +4 weeks, +3 months, +6 months, then visits will be every 6 months. Patients will arrive fasting, scheduled between 7-10am. Weight, blood pressure, heart rate and blood sampling is performed at each visit. A urine specimen will be collected at 3 time points. An ECG, (electrocardiogram) is performed at the second visit and repeated twice during the study. The OGTT with FPG and insulin level is completed every 12 months after baseline, at month 37(for confirmation), and as indicated to confirm progression to diabetes. Subjects are asked to keep a diary of suspected hypoglycemic events and a subset of patients may be provided a blood glucose monitor to record these occurrences. This study will include life style intervention counseling of subjects at every visit, with written educational materials provided by the study sponsor.

**Progress:** This protocol closed to patient entry 26 November 2003, with five subjects enrolled. Three subjects continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204045	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, multinational, multicenter, double-blind, randomized, active-controlled trial to compare the effects of Lotrel (amlodipine/benazepril) to benazepril and hydrochlorothiazide combined on the reduction of cardiovascular morbidity and mortality in patients with high risk hypertension, Protocol No. CCIB002I2301: ACCOMPLISH (Avoiding Cardiovascular Events through COMbination Therapy in Patients Living with Systolic Hypertension)		
<b>Principal Investigator:</b> MAJ Patricia A. Short, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jon C. Allison, MC; Michael R. Voorhies, PAC		
<b>Start - Completion:</b> 4/7/2004 - Oct 2009	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** (1) To assess the time to first event of composite cardiovascular morbidity and mortality with amlodipine/benazepril (Lotrel®) compared with the combination of benazepril and hydrochlorothiazide in patients with high risk hypertension. (2) To compare composite cardiovascular morbidity, new onset diabetes, progression of renal disease and hospitalization for congestive heart failure with amlodipine/benazepril (Lotrel®) versus the combination of benazepril and hydrochlorothiazide. (3) to compare all-cause mortality, all hospitalizations, renal function (estimated change in glomerular filtration rate), LVH, peripheral arterial revascularization procedure or nontraumatic amputation and progression/regression of microalbuminuria (30-300 mg/g) or clinical albuminuria (>300 mg/g) long term safety and tolerability with amlodipine/benazepril (Lotrel®) versus the combination of benazepril and hydrochlorothiazide. (4) To identify inherited genetic factors which may be related to hypertension, predict response to treatment with the study medications, predict relative susceptibility to drug-drug interactions, or predict genetic predisposition to serious side effects.

**Technical Approach:** This is a phase III randomized, multicenter, double-blind, parallel-group, active-controlled trial comparing the efficacy of amlodipine/benazepril combined therapy (Lotrel) to the combination of benazepril and hydrochlorothiazide (HCTZ) in high risk hypertensive subjects in reducing cardiovascular outcomes. 20 subjects may be enrolled at MAMC with approximately 12,600 worldwide. The study will last approximately 5 years, including the 18-month recruitment period. Eligible subjects will be randomized in 1:1 ratio to one of two groups to begin blinded treatment with amlodipine/benazepril 5/20 mg or benazepril 20mg/HCTZ 12.5 mg. The study provides for dose-titration followed by add-on therapy if necessary to achieve goal blood pressure (<140/<90 mmHg or lower in appropriate subjects).

Subjects will be followed every 4 weeks up to 3 months, at 6 months, and every 6 months thereafter. All randomized subjects will be followed until study completion, including those who interrupt or discontinue treatment. Additional visits may be done as needed to ensure blood pressure control. Patients will be treated in the study until the required number of randomized subjects with a primary cardiovascular event is achieved for analysis. Safety and efficacy assessments will consist of monitoring pre-defined non-serious adverse events, all serious adverse events, concomitant medications, regular monitoring of hematology and blood chemistry, urinalysis, vital signs and physical examinations. Observation for clinical endpoints will be continuous. Physical exams will focus on cardiovascular signs and symptoms. 12-lead ECG will be performed at baseline, month 18 and year 3. 24-hour ambulatory blood pressure monitoring at Year 2 will be done in a subset of subjects. Biomarker tests for high sensitivity C-reactive protein and other predictors of cardiovascular disease are scheduled. Subject participation in a pharmacogenetics sub-study is optional. A single blood specimen will be collected and DNA derived

from the sample may be stored and studied for up to 20 years by the study sponsor. Interim analyses for monitoring of efficacy demonstration and patient safety will be conducted by an independent Data Monitoring Committee.

**Progress:** This protocol closed to enrollment with 28 patients consented, 17 enrolled. Three subjects have discontinued taking study medication and all 17 continued to be followed during FY06.

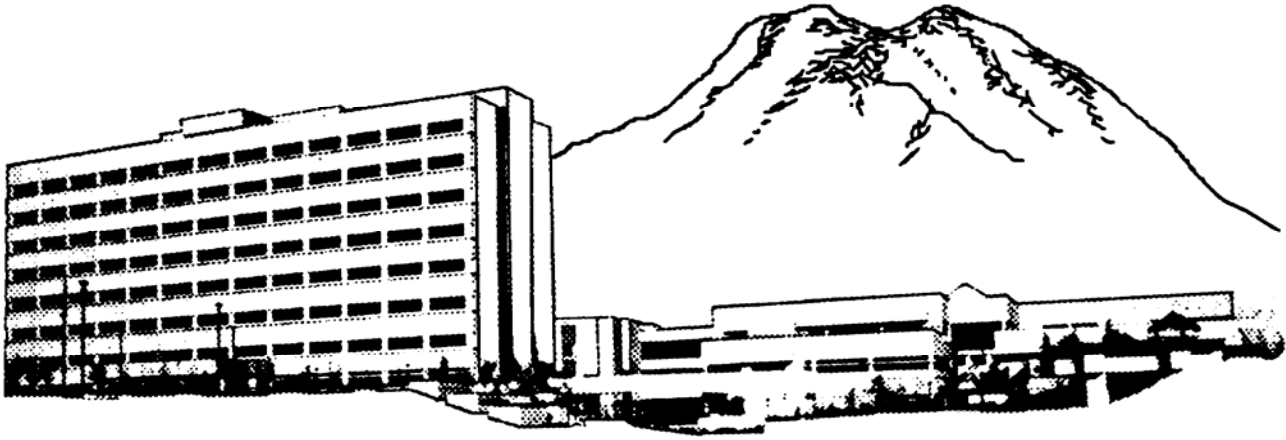
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205004	<b>Status:</b> Completed
<b>Title:</b> Efficacy of Iron in Restless Legs Syndrome (RLS) Patients With Low-Normal Ferritin: A Randomized, Double-Blind, Placebo Controlled Study		
<b>Principal Investigator:</b> CPT James Y. Wang, MC		
<b>Department:</b> Medicine/Internal Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Angela G. Mysliwiec, MC; CPT Collin J. Fischer, MC		
<b>Start - Completion:</b> 1/31/2005 - Aug 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/25/2005

**Study Objective:** To determine the efficacy of treating RLS patients who have low-normal ferritin with oral ferrous sulfate.

**Technical Approach:** This is a double blinded placebo-controlled study of iron in RLS patients that have a low-normal ferritin level (12-100mcg/l). Adult patients (age > 18) that meet the International RLS Study group diagnostic criteria for RLS will be consented to have a ferritin, iron panel, and CBC checked. Those who have concurrent ferritin in the low-normal range (12-100mcg/l) and at least moderately severe symptoms according to the IRLSSG rating scale for RLS will be eligible for the study. Sample size will be between 9-39 patients in each treatment group for a total of 18-78 patients. These patients will be randomized to treatment with 325mg iron twice a day by mouth or placebo. Patients will have follow up at 6 and 12 weeks post treatment. Outcome will be measured by improvement in overall score (decrease in total score by least 5 points) on the IRLSSG RLS validated severity survey from pre-treatment to 12 weeks post treatment and a statistical improvement of treatment group vs. placebo using the T test for independent samples. An additional endpoint measurement will be overall improvement in quality of life after treatment. Patients will be treated for a total of 12 weeks in this trial.

**Progress:** This protocol was reported completed in June 2006, with 38 subjects consented. Seventeen subjects completed the study, two left the area before completing, one did not think iron would benefit him, and eighteen screen-failed. No patients had significant adverse side effects from the study medication. Preliminary data analysis suggests that treating RLS patients with low-normal ferritin with PO iron may improve RLS symptoms and overall quality of life.



## **Detail Summary Sheets**

Nephrology Service, Department of Medicine



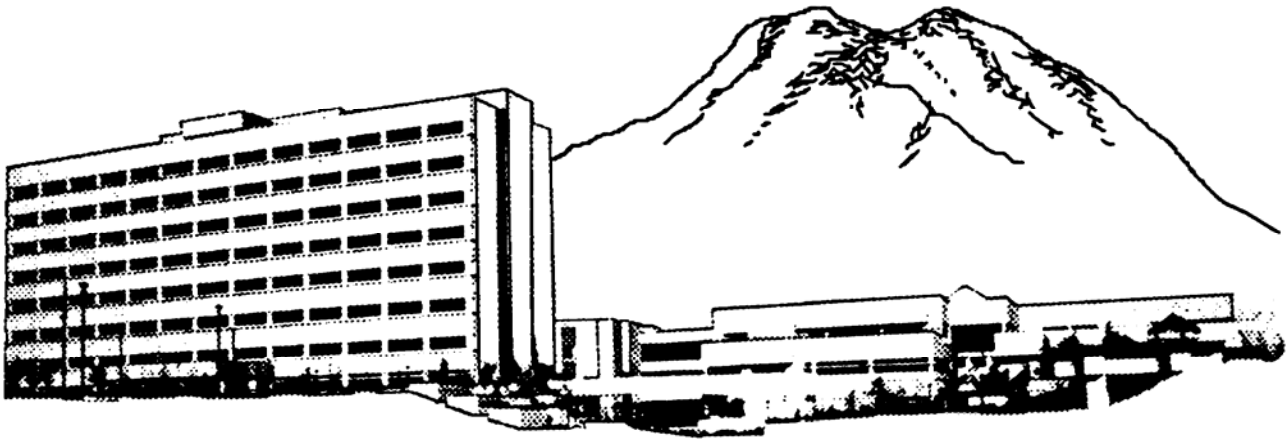
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205121	<b>Status:</b> Completed
<b>Title:</b> Does High Resistive Index by Doppler Ultrasonography Predict Small Kidney Sizes?		
<b>Principal Investigator:</b> MAJ Joseph Y. Lee, MC		
<b>Department:</b> Medicine/Nephrology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT David Owshalimpur, MC		
<b>Start - Completion:</b> 8/18/2005 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To retrospectively determine if high resistive indices by Doppler ultrasonography is predictive of small kidney sizes.

**Technical Approach:** This study is a retrospective review and data analysis of up to 400 Doppler ultrasound reports in the Vascular Clinic Lab database. Data recorded will include age, sex, percentage of renal artery stenosis (as reflected by aorta/renal artery velocity ratios), resistive index and kidney sizes. A review of ICDB medical records will be done to exclude the reports from patients who have a single kidney, diabetes, or infiltrative/cystic kidney disease. The control group will be ultrasound reports of patients who have no significant renal artery stenosis (>60%) or high resistive index (>80%). The resistive indices and kidney sizes will be grouped by age into this range: <30, 31-60, and >60. The control group will be divided the same way. Descriptive statistics will be used to summarize the overall sample. A correlation coefficient will be used to compare high resistive index to kidney size. Student's T-test will be used to compare mean kidney size of those with and without renal artery stenosis. A regression analysis will be used to determine the influence of resistive index, age, serum creatinine, GFR, and renal artery stenosis on kidney size.

**Progress:** This protocol was reported completed in April 2006. Results: There was no correlation between high renal resistive index and kidney size; nor any correlation between age, serum creatinine and male gender with kidney size. Both advancing age and serum creatinine were found to have smaller kidneys, while male gender compared to female gender had larger kidneys. Conclusion: This retrospective study did not show a correlation between renal resistive index, an indirect measure of small vessel kidney disease presumed to be caused by kidney sclerosis and kidney size.



## **Detail Summary Sheets**

Neurology Service, Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204062	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Trial of a Migraine Management Seminar in the Treatment of Migraines		
<b>Principal Investigator:</b> MAJ Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Beverly R. Scott, MC; Joan L. Wilson, MSW; CPT Douglas R. Langford, MC		
<b>Start - Completion:</b> 4/15/2004 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3/28/2006

**Study Objective:** To determine the effectiveness of a migraine management seminar for improving migraine headaches, migraine-associated disability and migraine-related quality of life.

**Technical Approach:** Subjects will attend a unique, 3-hour, single-session seminar to augment the medical management of migraine headaches. The seminar will educate subjects with migraines about their disorder and various treatments and teach practical non-pharmacologic migraine management skills. The study is a randomized, controlled, single-center trial to determine the efficacy of a migraine management seminar, when used as adjunctive therapy to standard medical therapy in the treatment of migraine headaches. Eighty subjects, fulfilling the International Headache Society criteria for migraines and suffering from significant migraine associated disability will be enrolled in the study. Subjects will be recruited from consecutive subjects referred to the MAMC Neurology Clinic for headache consultation. Study subjects will be randomized to medical therapy (control group) or medical therapy in combination with the migraine management seminar (treatment group). Medical therapy will be determined by each subject's consulting neurologist, will conform to standard of care for the treatment of migraine and not be constrained or otherwise influenced by the study. All subjects will record a standardized headache diary during the study period. The primary outcome measures are number of headache days per month and change in the Migraine Disability Assessment (MIDAS) score. Secondary outcomes include the Migraine Specific Quality of Life (MSQOL) questionnaire score, migraine severity and duration, healthcare utilization and a migraine management satisfaction survey. Outcomes will be assessed at baseline, 3 months after randomization and 6 months after randomization.

**Progress:** This protocol is open to enrollment 52 patients enrolled at MAMC. Twenty-six (26) patients have completed the study, seventeen remain actively enrolled, and nine were lost to follow-up. There have been no adverse outcomes. No data analysis has been done.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 203048	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Trial of B Vitamins for Alzheimer's Disease			
<b>Principal Investigator:</b> MAJ Jay C. Erickson, MC			
<b>Department:</b> Medicine/Neurology			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Frederick G. Flynn, MC			
<b>Start - Completion:</b> 6/8/2004 - Mar 2005	<b>Funding:</b> Upsher-Smith Laboratories via Henry M. Jackson Foundation		<b>Periodic Review:</b> 1/24/2006

**Study Objective:** To determine whether B vitamin supplements improve cognitive function in patients with mild-to-moderate Alzheimer's disease.

**Technical Approach:** To test the hypothesis that B vitamin supplements improve cognitive function in patients with Alzheimer's disease, 80 patients with mild-to-moderate Alzheimer's disease will be enrolled in a prospective, randomized, open-label trial. Subjects will be randomized to receive B vitamin supplements consisting of vitamin B12 (0.5 mg qd), vitamin B6 (50 mg qd), and folate (2 mg qd) or no B vitamin supplements over a period of 1 year. Cognitive function, as measured by the Alzheimer's Disease Assessment Scale (ADAS), will be measured at baseline and then after 3 months, 6 months, and 12 months of treatment. The primary outcome will be change in ADAS score compared to baseline. Analysis of variance will be used to test for significant differences between the two treatment groups.

**Progress:** This protocol remains open to enrollment, with six subjects enrolled, one during FY06. Five subjects have completed participation, and one subject continued to be followed. No adverse events have occurred.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206075	<b>Status:</b> Ongoing
<b>Title:</b> Association Between Migraine and Psychiatric Conditions In Soldiers Returning from Combat		
<b>Principal Investigator:</b> MAJ Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Gregory A. Gahm, MS; Barbara A. Lucenko, PhD;		
<b>Start - Completion:</b> 4/4/2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objectives: To determine the prevalence of post-traumatic stress disorder (PTSD) among Soldiers with and without migraine headaches, to determine the prevalence of depression among Soldiers with and without migraine headaches. to determine the association between PTSD and migraine outcomes in Soldiers, and to determine the association between depression and migraine outcomes in Soldiers.

**Technical Approach:** PHQ-9 and PC-PTSD scores will be obtained from the SWAP database for each subject enrolled in the migraine screening database. A single database will be constructed.

**Progress:** This protocol is closed to patient entry, with a total of 2,605 subjects enrolled in this cross-sectional, observational study. The protocol remains ongoing for data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203097	<b>Status:</b> Ongoing
<b>Title:</b> CLOSURE I Trial: A Prospective, Multicenter, Randomized, Controlled Trial to Evaluate the Safety and Efficacy of the STARFlex Septal Closure System Versus Best Medical Therapy in Patients with a Stroke and/or Transient Ischemic Attack Due to a Presumed Paradoxical Embolism Through a Patent Foramen Ovale		
<b>Principal Investigator:</b> MAJ Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Beverly R. Scott, MC; COL David T. Schachter, MC; CPT Erik K. Helseth, MC		
<b>Start - Completion:</b> 9/18/2003 - Oct 2006	<b>Funding:</b> NMT Medical, Inc via Henry M. Jackson Foundation	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** To determine whether the STARFlex Septal Closure System (STARFlex) will safely and effectively prevent recurrent embolic stroke/transient ischemic attack (TIA) and mortality in patients with a patent foramen ovale (PFO) and to demonstrate superiority of the STARFlex device compared to best medical therapy.

**Technical Approach:** The STARFlex Septal Closure System is an investigational device for non-surgical, transcatheter closure of intracardiac defects. The CLOSURE I Trial is a prospective, multicenter, randomized, controlled trial to evaluate the safety and efficacy of the STARFlex System in preventing recurrent cerebrovascular events in patients with a PFO. The study will enroll MAMC patients 18 to 60 years of age who have had a documented stroke or TIA within the last 3 months, have a PFO as detected by transesophageal echocardiography (TEE) with saline contrast bubble study, and do not have any other potentially embolic source or other cause of stroke or TIA. Up to 15 patients will be enrolled at MAMC and a total of 1600 patients will be enrolled at 120 centers in the United States. Investigators will receive training in use of the device. Patients will be randomized to receive implantation of the STARFlex device with concomitant aspirin therapy or medical therapy consisting of aspirin and/or coumadin. Patients who have device implantation will also be treated with clopidogrel (Plavix) 75mg daily for 6 months. All patients will undergo serial physical exams, EKGs, and neurological evaluations (to detect recurrent stroke or TIA) at 6 months, 12 months, and 24 months after device implantation or initiation of medical therapy. Patients who receive the device will also have a transesophageal echocardiogram with saline contrast bubble study and chest x-ray 6 months after implantation to assess for closure of the PFO and condition of the device. The primary endpoints of the study are the 2-year incidence of stroke/TIA and all cause mortality. Data will be analyzed on an intent-to-treat basis using the chi-square test and logistic regression. A central Data and Safety Monitoring Board will inspect and make recommendations regarding rate of stroke/TIA at approximately 10 months and 18 months after start of the study for efficacy or safety concerns.

**Progress:** This protocol remains open to enrollment with three volunteers enrolled in the last twelve months, bringing the total number of enrolled subjects to eight. Four subjects were randomized to the STARflex device arm and four subjects were randomized to the medical therapy arm. Two subjects have moved away from the area and will complete study participation at another research site. Six subjects continued to be followed at MAMC during FY06. The STARflex device became dislodged in one subject during the implantation procedure, requiring surgical removal, but there were no long-term complications.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205107	<b>Status:</b> Completed
<b>Title:</b> Diagnosis and Treatment of Migraines in U.S. Army Soldiers		
<b>Principal Investigator:</b> MAJ Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Douglas R. Langford, MC		
<b>Start - Completion:</b> 7/21/2005 - Sep 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To determine the proportion of soldiers with migraines whose headaches are diagnosed as migraines prior to neurology consultation. (2) To determine the prevalence of analgesic overuse among soldiers with migraine. (3) To determine the medical treatment provided to soldiers with migraines.

**Technical Approach:** A retrospective chart review will be performed to determine the patterns of medical care provided to Army soldiers with migraine headaches. The charts of 50 consecutive active duty Army soldiers meeting International Headache Society diagnostic criteria for migraine headaches who were evaluated in the MAMC neurology clinic in 2004 will be reviewed. Diagnosis and treatments prior to, and after, neurology consultation will be compared. Endpoints will include the proportions of patients diagnosed with migraine, treated with prophylactic medications, treated with triptan-class medications, and treated with non-pharmacologic treatments.

**Progress:** A total of 50 Soldiers participated. A diagnosis of migraine was made in 42% of patients prior to neurology referral and in 100% upon neurology consultation ( $p < 0.001$ ). Analgesic overuse was diagnosed in 0% of patients before neurology consultation and in 23% at the time of neurology consultation ( $p < 0.001$ ). 63% of eligible patients were treated with a prophylactic medication prior to neurology referral compared to 100% after neurology consultation ( $p < 0.01$ ). Prior to neurology referral, acute migraine treatment using combination analgesics or opioids was significantly more common ( $p < 0.001$ ) and treatment using a triptan medication was significantly less common ( $p = 0.003$ ). Non-pharmacologic treatments for migraine were used in 4% of patients before neurology referral and in 52% after neurology consultation.

**Conclusions:** Migraine headaches are frequently undiagnosed in Soldiers prior to neurology consultation. Concomitant analgesic overuse affects nearly one quarter of Soldiers with migraines at the time they are first seen in neurology, but is rarely recognized prior to referral. Soldiers with migraines are less likely to be treated with prophylactic medication, migraine-specific medications, or non-pharmacologic treatments prior to neurology consultation. Improving the ability of first-line providers to diagnose and treat migraine will reduce the burden of this disorder in Soldiers and thus enhance military readiness.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205118	<b>Status:</b> Ongoing
<b>Title:</b> Prevalence and Impact of Migraine Among Deployed Soldiers		
<b>Principal Investigator:</b> MAJ Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Brett J. Theeler, MC		
<b>Start - Completion:</b> 8/5/2005 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7/18/2006

**Study Objective:** (1) To determine the prevalence of migraine among soldiers during military deployment. (2) To determine the frequency and severity of migraine headaches among deployed soldiers. (3) To determine the impact of migraines on soldier readiness during deployment. (4) To determine the diagnosis and treatment patterns of migraine among deployed soldiers.

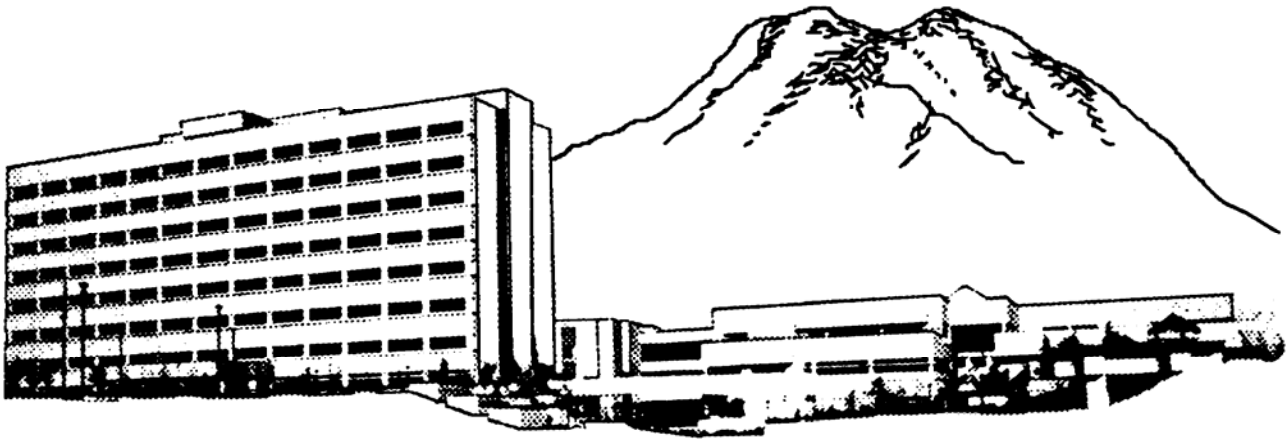
**Technical Approach:** This is a cross-sectional, observational, questionnaire based study to determine the prevalence, impact, and treatment patterns of migraine among soldiers during military deployment. Approximately 3,000 soldiers of the 1st Stryker Brigade will be asked to voluntarily complete a standardized, validated, headache questionnaire during their post-deployment health evaluation. The questions on the questionnaire are based on the diagnostic criteria of migraine, headache frequency, headache-related disability, and headache treatments. Responses will be used to calculate the prevalence, frequency, severity, and duration of migraines among deployed soldiers. The extent to which migraines impede performance of military duties and current treatment patterns for migraine among this population will also be determined. Dependent variables include: proportion of soldiers experiencing one or more migraine headaches during deployment; mean number of headache days per month; mean duration and severity of headaches; number of missed and sub-optimal duty days attributable to headache; proportion of soldiers with migraine who were previously diagnosed by a healthcare provider and proportion of soldiers with migraine who used migraine-specific medications during deployment.

**Progress:** The study questionnaire was completed by 2,725 Soldiers; 377 Soldiers with migraines subsequently completed a follow-up questionnaire three months later. Data analysis is almost complete. Preliminary results were presented at the American Headache Society meeting 24 June 2006.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205115	<b>Status:</b> Ongoing
<b>Title:</b> Study of Acute Viprinex™ for Emergency Stroke: A Randomized, Double-Blind, Placebo-Controlled Study of Viprinex™ (Ancrod Injection) in Subjects Beginning Treatment within 6 Hours of the Onset of Acute, Ischemic Stroke		
<b>Principal Investigator:</b> MAJ Jay C. Erickson, MC		
<b>Department:</b> Medicine/Neurology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Robert B. Blankenship, MC; MAJ Anna D. Hohler, MC; CPT Jessica D. Lee, MC; CPT Douglas R. Langford, MC; MAJ Jason A. Friedman, MC; CPT Erek K. Helseth, MC; COL Beverly R. Scott, MC		
<b>Start - Completion:</b> 11/9/2005 - Sep 2007	<b>Funding:</b> Neurobiological Technologies, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 7/20/2006
<b>Study Objective:</b> To determine whether ancrod (Viprinex™) begun intravenously within 6 hours of stroke onset confers statistically benefit in reducing the incidence of disability at 90 days		
<b>Technical Approach:</b> This is a phase III, double-blind, placebo controlled study to that will be conducted by the Neurology/Stroke Team service at MAMC. Up to 10 subjects may be enrolled; a total of 500 enrolled in the study overall. Eligible subjects will present to the ER with the diagnosis of a stroke and symptom onset within 6 hours before the Ancrod infusion. If patients are eligible to receive rt-PA, they will not be enrolled in this study. Subjects will have a routine history and physical, neurological examination, laboratory tests, a non-contrast CT scan, and a 12 lead ECG. Subjects will be randomized to one of two treatment groups in a biased-coin approach using study-wide balanced enrollment in the two treatment groups by age category (<65, 65-75, >75), independent of stratum assignment. Randomization will be completed via an interactive voice response system. Subjects will receive the 3 hour transfusion and continue to have follow-up after discharge until 90 days after being treated with study medication.		
<b>Progress:</b> This protocol remains open to patient entry. No patients have met enrollment criteria. Study staff continues to actively screening all acute stroke patients.		



## **Detail Summary Sheets**

Pulmonary Disease & Critical Care Service,  
Department of Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205032	<b>Status:</b> Terminated
<b>Title:</b> Adjunctive Role of Mirtazapine in Mild Positional Sleep Apnea		
<b>Principal Investigator:</b> LTC (Ret) William E. Caras, M.D.		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Bernard J. Roth, MC; MAJ Vincent Mysliwiec, MC; Larry G. Knauss, Ph.D.		
<b>Start - Completion:</b> 10/11/2005 - Nov 2005	<b>Funding:</b> Oraganon via The Geneva Foundation	<b>Periodic Review:</b> 1/18/2006

**Study Objective:** This study plans to look at the adjunctive role of Mirtazapine, an antidepressant with sleep enhancing qualities, to positional therapy (PST) in patients with mild positional OSA.

**Technical Approach:** This is a prospective randomized placebo controlled trial. 30 subjects will be enrolled following screening and randomized to receive active drug or placebo. Both groups will be asked to complete a sleep diary. PSG variables will be total sleep time, sleep efficiency, sleep latency, Stage 1 sleep, Stage 2 (min) Stage 3(min), Rem (min), Rem latency (min). Amended: Jan 2006, to an open, sequential design to allow all potential patients to enroll in the 1st phase of the study, which will use only the positional sleep vest. After a month of treatment patients will be reassessed and then may chose to enroll in the 2nd phase of the study combining the sleep vest with Mirtazapine.

**Progress:** This study was amended in January 2006, to an open, sequential design to allow all potential patients to enroll in the first phase of the study using only the positional sleep vest. After a month of treatment patients would be reassessed and then may chose to enroll in the second phase of the study combining the sleep vest with Mirtazapine. However, Dr. Caras eventually terminated the study due to lack of accrual citing patient's deep seated reluctance to take a medication known as an antidepressant.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206083	<b>Status:</b> Terminated
<b>Title:</b> A Randomized, Double-blind, Placebo-controlled, Parallel Group, Stratified, Multi-center, 12 Week Study Comparing the Safety and Efficacy of Fluticasone and Formoterol Combination (FlutiForm™ 100/10 mcg twice daily) in a Single Inhaler (SkyePharma HFA pMDI) with the Administration of Placebo or Fluticasone (100 mcg twice daily) and Formoterol (10 mcg twice daily) Alone in Adolescent and Adult Patients with Mild to Moderate Asthma		
<b>Principal Investigator:</b> LTC Cynthia L. Clagett, MC		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Alexander S. Niven, MC; CPT Katherine A. Simonson, AN		
<b>Start - Completion:</b> 6/28/2006 - Dec 2007	<b>Funding:</b> SkyePharma via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective is to demonstrate the efficacy of SKP FlutiForm HFA pMDI compared to Fluticasone propionate and Formoterol fumarate alone and placebo when administered by inhalation twice daily over 12 weeks in adult patients with mild to moderate asthma. (Only subjects 18 years or older with mild asthma will be enrolled at MAMC)

**Technical Approach:** All eligible patients will undergo a Run-In Period of up to 2 weeks depending on their history of steroid use. Steroid-requiring patients will undergo a Run-In Period up to 2 weeks during which they will receive asthma maintenance therapy using Fluticasone HFA pMDI (50 mcg twice daily). Steroid-free patients will undergo a Run-In Period up to 4 weeks during which they will not receive any controlling medication. Use of rescue Albuterol pMDI will be permitted for all patients as needed for the control of worsening asthma symptoms during the Run-In period. At the Baseline Visit (Week 0) following the Run-In period, eligible patients will be randomized to the treatment groups. Treatment assignment will be stratified according to prior steroid use (steroid-requiring versus steroid free). Study drug will be administered twice daily over a 12 week period. Patient visits will occur at Weeks 2, 4, 8 and 12, during which assessments (including serial PFTs up to 4 hours) will be made. During the Treatment Period, patients may take only their blinded study medication; all other asthma medications will be withheld for the duration of the Treatment Period. Use of the rescue Albuterol pMDI will be permitted in all patients as needed during the Treatment Period for control of worsening asthma symptoms.

**Progress:** This protocol was terminated 21 September 2006, due to failed contract negotiations with the study sponsor. The study was never initiated at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206086	<b>Status:</b> Ongoing
<b>Title:</b> Identifying Adherence Obstacles to CPAP Therapy		
<b>Principal Investigator:</b> MAJ Vincent Mysliwiec, MC		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Robert D. Swanson, M.A.; Suzette Gagnon-Bailey, RN; Michael J. Kuculyn; Richard D. Guesford		
<b>Start - Completion:</b> 5/8/2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to introduce a survey, in the form of a Concerns Questionnaire that will assess compliance and reasons for non-compliance in patients diagnosed with Obstructive Sleep Apnea (OSA) who are prescribed Continuous positive airway pressure (CPAP).

**Technical Approach:** Subjects with OSA that will be treated with CPAP will be identified by treating provider and scheduled for follow up within 3 months. Subjects will return for follow up with the downloaded data from CPAP machine and compliance data downloaded. During this time patients will complete the "PAP Concerns Questionnaire." The downloaded data are transferred to "CPAP Concerns Questionnaire" for analysis.

**Progress:** Data collection is complete with 100 patients who utilize CPAP having filled out the questionnaire during FY06. Data has been entered into a excel spread sheet and is ready for interim analysis. At this point we plan to identify which specific questions are statistically significant in determining CPAP compliance.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205128	<b>Status:</b> Ongoing
<b>Title:</b> Impulse Oscillometry and Obstructive Lung Disease: Assessment of a Clinically Significant Bronchodilator Response		
<b>Principal Investigator:</b> MAJ Alexander S. Niven, MC		
<b>Department:</b> Medicine/Pulmonary & Critical Care		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Steven P. Bennett, MC; LTC Cynthia L. Clagett, MC; CPT Johathan R. Coyle, MC; Suzette Gagnon-Bailey, RN; MAJ William F. Kelly, MC; MAJ Vincent Mysliwicz, MC; MAJ John P. Rinard, MC; CPT Charles C. Broy, MC		
<b>Start - Completion:</b> 12/14/2005 - Sep 2008	<b>Funding:</b> Amarillo Pulmonary via MAMC	<b>Periodic Review:</b> 9/26/2006

**Study Objective:** This study will (1) evaluate asymptomatic nonsmokers using impulse oscillometry (IOS) and conventional pulmonary function tests before and after bronchodilator administration to determine the normal adult bronchodilator IOS responses to albuterol and (2) evaluate the ability and extent to which IOS can identify airway changes in asymptomatic smokers, patients with asthma and chronic obstructive lung disease (COPD) compared to standard pulmonary function testing.

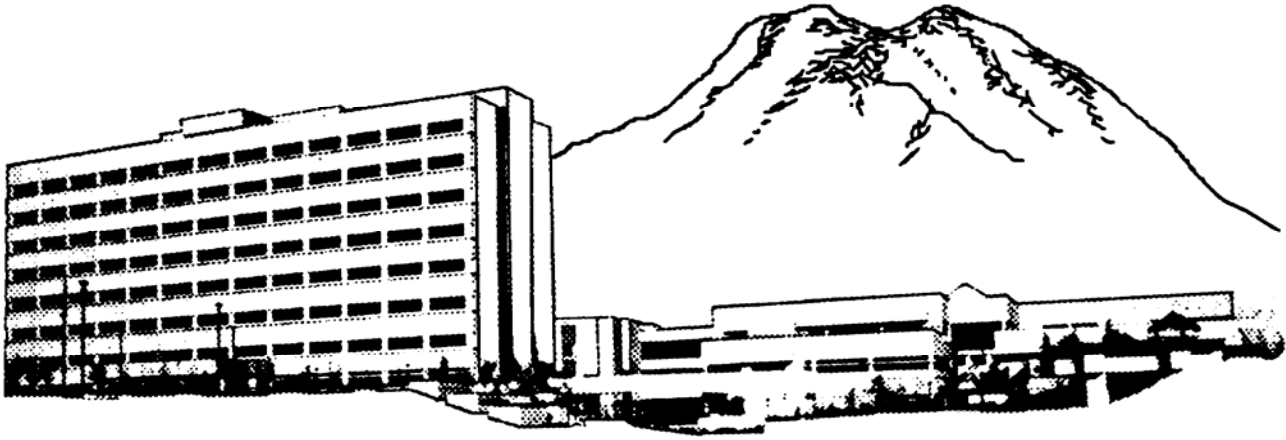
**Technical Approach:** 89 asymptomatic nonsmoker volunteers will be recruited from the hospital staff. 89 asymptomatic smokers will be recruited from the hospital staff and family members of patients visiting Madigan AMC for medical appointments. Based on prior literature suggesting that 50% of asthmatics and 10-15% of COPD patients will have evidence of reversible airway obstruction, 178 asthmatics and 890 patients with COPD will need to be enrolled to examine this important variable. These subjects will be recruited from routine outpatient referrals to the Pulmonary Function Lab for clinical testing.

All asymptomatic subjects will complete a questionnaire on their demographics, medical and smoking history, and a review of systems to confirm the absence of cardiopulmonary complaints. Height, sitting height, and weight will be measured in each subject. Four IOS measurements of 60-90 seconds each will be performed followed by standard spirometry and lung volume measurements. Each subject will receive 3 inhalations of albuterol 90 micrograms using a spacer device and repeat the IOS, spirometry, and lung volume measurements after 10 minutes. Subjects with asthma and COPD will undergo the same protocol, with the addition of completing a validated asthma or COPD questionnaire to evaluate the severity and impact of their respiratory disease on their daily activities.

The primary outcome variables for IOS will include the respiratory impedance (Zrs), respiratory resistance at 5, 15, and 20 Hz (R5, R15, R20), frequency dependence from 5-15 Hz and 5-20 Hz (R5-15, R5-20), the respiratory reactance at 5 Hz (X5) and the reactance area (AX), the resonant frequency (frs) before and after bronchodilator administration. The primary outcome variables for conventional pulmonary function testing will be the forced vital capacity (FVC), the forced expiratory volume in 1 second (FEV1) and 6 seconds (FEV6), the ratio of FEV1 to FVC, body plethysmography measurements for functional residual capacity (FRC), inspiratory capacity (IC), and vital capacity (VC) before and after bronchodilator administration. Summary statistics, frequency and/or contingency tables will be provided for all variables of the study. Baseline and post-bronchodilator IOS variables will be correlated to conventional pulmonary function measurements using a paired t test. The impact of variables age, height, sitting height, race, gender, and allergy symptoms will be evaluated using the Analysis of Variance (ANOVA) and the Multivariate Analysis of Variance (MANOVA). Comparison between measurements obtained in asymptomatic nonsmokers and measurements obtained in asymptomatic smokers, asthmatics and

COPD subjects will be performed using ANOVA. Pearson's R correlations between IOS measurements, conventional pulmonary function measurements, and questionnaire based symptom scores will be obtained and the impact of the variables listed above will also be evaluated.

**Progress:** This protocol remains open to patient entry, with twelve subjects enrolled in the past eight months (Asthma (1), COPD (4), and no lung disease (7). The information obtained in this study is from a single visit; no follow up is required unless a new diagnosis is discovered. Of the arms in the study actively enrolling, no new diagnoses have been found. Patient recruitment continues, but has been difficult due to frequent deployments and staff and technician shortages.



# Detail Summary Sheets

## Nutrition Care Division



## Detail Summary Sheet

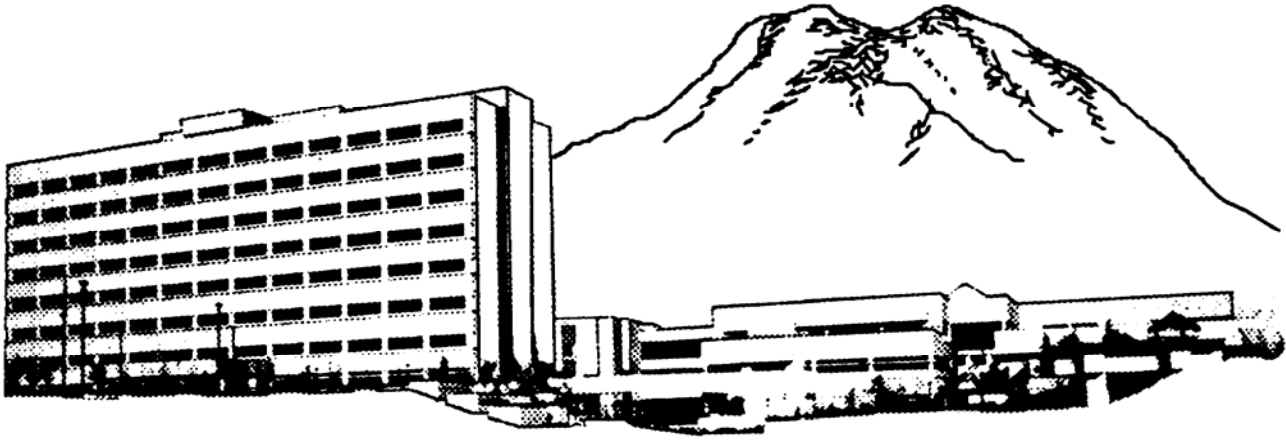
<b>Date:</b> 30 Sep 06	<b>Number:</b> 206008	<b>Status:</b> Ongoing
<b>Title:</b> Attenuation of Exertional Muscle Damage with a Nutritional Supplement		
<b>Principal Investigator:</b> Colleen Cates-Gorang, R.D., CDE		
<b>Department:</b> Nutrition Care	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Leslee F. Sanders, MC; Patricia A. Deuster, PhD; MAJ Steven D. Mahlen, MS; CPT Eric Grenier, SP; CPT Michael J. Hartenstine, MS		
<b>Start - Completion:</b> 2/9/2006 - Aug 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/26/2006

**Study Objective:** Determine the extent to which ingestion of a carbohydrate (CHO)-electrolyte beverage with essential amino acids (EAA) to include glutamine, by soldiers during and after strenuous exercise prevents exertional muscle damage (EMD) as compared to a carbohydrate-electrolyte beverage alone. Biochemical analysis will include measuring plasma markers of damage such as creatine kinase (CK) and interleukin-6 (IL-6), blood in urine and subjective measurements of pain in a group of soldiers before, after, and 48 hours after a strenuous military training event.

**Technical Approach:** The study will be a randomized, double-blind, crossover design utilizing Fort Lewis soldiers as the study population. Subjects will be divided into two groups of a minimum of ten per group and assigned to one of two treatment conditions, either receiving a placebo beverage or the treatment beverage. Both beverages will be manufactured by the Gookinaid Company per the following specifications: the placebo beverage will contain 45-60 grams of carbohydrate per liter, 270 milligrams of sodium and 400-500 milligrams of potassium providing a calorie range of 180-240 per liter (similar to a commonly available sports drink such as Poweraid); the treatment beverage will consist of the placebo plus 5 grams per liter of essential amino acids and 3.5 grams per liter of glutamine and provide 215-275 calories per liter (equivalent to adding a glutamine powder such as ProLab Glutamine® to a sports beverage or utilizing a sports beverage such as Growling Dog Replacement Drink®, both widely available for purchase).

The subjects will participate in a 7 ½ mile road march carrying a backpack weighted to 30% of his/her body weight (up to a maximum of 83 pounds) - or an event similar in difficulty level. A minimum of 1 liter of beverage will be ingested each hour during the event and an additional 1 liter of beverage consumed within two hours afterwards. After a 7-14 day washout period, the event will be repeated, with the subjects consuming the alternate beverage; each subject is acting as his/her own control to determine difference in treatment effect. Within subject and between treatment group comparisons will be performed using ANOVA. Performance, metabolic and muscle damage response data will be evaluated with repeated-measures ANOVAs and t-tests. Dietary intake of specific nutrients will be estimated for each subject using the 4-day food record, (previously validated and utilized at the University of Washington) and analyzed with software from the University of Minnesota - Nutrient Data System for Research (or similar software).

**Progress:** Thus far, 33 Soldiers have completed both phases of study since protocol approval. Data analyses are on-going, with aliquots currently stored for approved future laboratory analyses, as funding allows. Statistical analyses are pending.



# Detail Summary Sheets

Department of Nursing

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206093	<b>Status:</b> Ongoing
<b>Title:</b> Effects on Aspirated Volume, Patency, and Tracheal Mucosa using High Intermittent Negative Pressure versus Low Continuous Negative Pressure for Subglottic Secretion Aspiration		
<b>Principal Investigator:</b> Charlotte L. DePew, RN, MSN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Cynthia L. Clagett, MC; MAJ Steven P. Bennett, MC; Mary S. McCarthy, RN, PhD; Nora A. Regan, CRT; MAJ William F. Kelly, MC; MAJ Alexander S. Niven, MC; MAJ Jeffrey B. Musser, MC		
<b>Start - Completion:</b> 8/1/2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A
<b>Study Objective:</b> Objectives: To determine the effect on aspirated secretion volume using high intermittent versus low continuous subglottic secretion aspiration with the HiLo Evac endotracheal tube. To determine the effect on line patency using high intermittent versus low continuous subglottic secretion aspiration with the HiLo Evac endotracheal tube. To describe the effect on tracheal mucosa using photographic images obtained endoscopically when evaluating high intermittent versus low continuous subglottic secretion aspiration with the HiLo Evac endotracheal tube.		
<b>Technical Approach:</b> This study will use a prospective, quasi-experimental design to answer the important questions about maintaining line patency, effectively removing secretions, and minimizing mucosal trauma from applied negative pressure. Sixty subjects will be required with 30 per group receiving either low continuous suction or high intermittent suction. Method of suction will alternate each month for 6 months. Patients will be included if they require mechanical ventilation for longer than 3 days. At that point consented patients will receive a baseline video-assisted tracheoscopy at the time of their routine subglottic suctioning intervention. Mucosal trauma will be graded according to the Modified Mathias-Wedley Tool. From that point on, patients will receive a once daily video-assisted tracheoscopy every one to three days with grading of any mucosal injury. A secretion specimen taken during the tracheoscopy from above the cuff will be submitted for microbiologic examination. Patency and secretion volume aspirated will also be recorded daily. Data will be analyzed by Student's t test for group comparisons and ANOVA/ANCOVA for individual / group comparisons over time. The results will be used to finalize the evidence-based practice protocol for prevention of VAP in the MAMC ICU.		
<b>Progress:</b> This protocol is open to patient entry, with no patients enrolled during FY06. Study staff have asked Department of Anesthesia to add the HiLo Evac ETT to their emergency intubation bags. Several opportunities for enrollment were missed since Anesthesia often uses their own ETT for emergent intubation.		

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203030	<b>Status:</b> Completed
<b>Title:</b> Junior Army Nurse Corps Officers' Perceptions, Experiences and Expectations of Head Nurse Leadership		
<b>Principal Investigator:</b> MAJ Jean M. Jones, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, Ph.D.; CPT Linda L. Blackman, AN; COL (Ret) Eileen A. Hemman, PhD		
<b>Start - Completion:</b> 5/16/2003 - Oct 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/12/2006

**Study Objective:** Describe Junior Army Nurse Corps Officers' perceptions, experiences, and expectations of head nurse leadership at Madigan Army Medical Center.

**Technical Approach:** Selected Participants will be will be mailed information on the research study approximately 3 weeks prior to the anticipated start date of the study through MAMC distribution. Those volunteering to participate will be scheduled for attendance at focus group sessions through telephone calls made by non military administrative personnel in the Nursing Research Office 10 to 14 days prior to the session. Each focus group session will last up to 120 minutes to include administrative time for informed consent, preliminary instructions, and answering participant questions. All focus group interviews will take place in a site in the hospital. Focus groups will begin by the moderator introducing the agenda and sharing ground rules for participation. Comments generated from the focus group discussions will be recorded using an audio tape recorder and one other research team member (the PI, CI, SC and/or RA) will be a non-participant observer. The facilitator will guide and focus the group discussion and interaction, while the observer will record the discussion, note participants' interaction patterns and non-verbal responses as additional data. Additional field notes will be written when the facilitator and the non-participant observer debrief after each focus group.

**Progress:** The final Head nurse (HN) focus group was held and data were analyzed using Husserlian descriptive phenomenology, predominately Collazzi's approach. HN leadership characteristics that positively impact Junior Officer (JO) retention included: (1) HNs that have a desire to serve in the HN Role, are clinically competent and administratively effective, counsel per standards and provide career development guidance, provided fair and equitable schedules for civilian and military staff, use the ANC Lifecycle as a tool to guide careers (However the Lifecycle should be based on today's optempo, include more TO&E positions and a clinical track.), mentor JOs early, and provide recognition based on performance and achievement, not rank; and (2) Senior leaders that mentor and develop HNs, provide realistic HN preceptorships, select HNs based on recommendations and resumes, and only selecting the best of the best.

The study identified significant differences between HN and Junior ANC Officer perceptions that also may negatively impact retention including: (1) Counseling-HNs perceived that JOs wanted lengthy counseling. JOs wanted HNs to counsel quarterly and provide career guidance; (2) Mentoring-HNs attempted to mentor JOs by giving them jobs like Schedule, Performance or Education Coordinator to help develop leadership skills. JOs said HNs didn't know how to properly mentor and they did not view HN delegated jobs as career enhancing; (3) Recognition-HNs perceived that JOs want more public recognition. JOs wanted acknowledgement based on the achievement, not rank; and (4) Scheduling-HNs perceived that JOs didn't want to work night or weekend shifts or more than forty hours per week. JOs said their concern was the disparity between civilian staff's empowerment to get desired schedules and military nurses' lack of a voice when scheduling issues arose.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205117	<b>Status:</b> Ongoing
<b>Title:</b> A Qualitative Descriptive Study that Identifies Essential Competencies and Leadership Characteristics of Army Adult Medical-Surgical Critical Care Head Nurses (dissertation)		
<b>Principal Investigator:</b> Lori A. Loan, RNC, Ph.D.		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Roy A. Harris, AN		
<b>Start - Completion:</b> 7/29/2005 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7/10/2006

**Study Objective:** The purpose of this study is to identify and describe competencies and leadership characteristics of Army Adult Medical-Surgical Critical Care Head Nurses. The research questions are: (1) what are the essential competencies and leadership characteristics identified by Army Critical Care Head Nurses themselves, (2) what are the essential competencies and leadership characteristics of Army Critical Care Head Nurses identified by Army critical care staff nurses, (3) what are the essential competencies and leadership characteristics of Army Critical Care Head Nurses identified by Army Chief Nurses, and (4) what common essential competencies and leadership characteristics of Army Critical Care Head Nurses do these three levels of professional nursing identify?

**Technical Approach:** This is a qualitative, descriptive study semi-structured interviews that include both closed-ended and open-ended questions as the primary means of data collection. Five Army Nurse Corps nurses will be asked to participate at MAMC; the Chief Nurse, one Critical Care Head Nurse, and three Critical Care staff nurses. Total study subjects from all sites will be 35; 5 nurses each from Walter Reed Army Medical Center, Landstuhl Regional Medical Center, Dwight David Eisenhower Army Medical Center, Tripler Army Medical Center, Brooke Army Medical Center, William Beaumont Army Medical Center, and Madigan Army Medical Center. The associate investigator will conduct the interviews in all seven medical centers and at all echelons. Documented informed consent will be obtained to allow subjects to decline enrollment. The consent process will not be conducted by the associate investigator who will be conducting the interviews.

Demographic data will be collected which will serve as a descriptive framework during the analysis phase of the study. Frequencies and measures of central tendency will be utilized to analyze the respondent's demographic data. Other analyses will be conducted using descriptive qualitative methodology. Qualitative analysis of the data will be completed with a focus on a comprehensive description of essential competencies and leadership characteristics of Army Critical Care Head Nurses as perceived by the three echelons of respondents. To ensure that ongoing analysis occurs throughout the study, the modality of constant comparative analysis will be utilized. The data will be organized by transcribing the audiotapes of the interviews into the Microsoft word processing program. The transcriptions will be entered into the computer program, NVivo to facilitate the coding process. Information gleaned from this study will be de-identified and aggregated and used as part of the associate investigator's dissertation requirement at George Mason University. Findings will also be offered to the Army Nurse Corps, presented at nursing conferences and published in a national nursing journal.

**Progress:** Data collection is completed with a total of 30 interviews from 6 different Army Medical Centers. IRB approval at Tripler Army Medical Center took much longer than other IRBs and therefore the timeline became too long to complete research in a timely manner for completion of dissertation this Fall. After discussion with Dissertation Chair and committee, it was decided that 30 interviews from the remaining medical centers was sufficient to achieve saturation. All 30

interviews are completed and transcribed. All interviews have been sent to the interviewees for review and comment (per proposal) and 20 have been returned. The transcripts, tapes and notes are all secured in accordance with the proposal. There have been no complaints from any of the interviewees either during the interview process or afterwards. Many expressed tremendous enthusiasm in participation and were very interested in findings. This study is entering data analysis that will utilize the NVivo 7 program. The three basic skill sets of technical, human and conceptual (Katz) become the foci of sorting responses (per proposal). Data analysis will look at responses to each question and a comparison within each echelon of leadership as well as the contrasts between the echelons of nursing leadership. Anticipated conclusion of study is Fall 2006.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202066	<b>Status:</b> Ongoing
<b>Title:</b> Caring Interventions for Couples Who Have Miscarried		
<b>Principal Investigator:</b> Lori A. Loan, RNC, Ph.D.		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Kristen M. Swanson, RN, Ph.D., FAAN; Mark A Biernbaum, Ph.D.; Kathryn Barnard, RN, Ph.D., FAAN; Martha J. Lentz, BSN, MN, Ph.D.; Margaret M. Heitkemper, Ph.D.		
<b>Start - Completion:</b> 5/16/2002 - Oct 2004	<b>Funding:</b> NIH via MIPR	<b>Periodic Review:</b> 5/9/2006

**Study Objective:** The purpose of this randomized study is to compare the effects of nurse caring (3 nurse counseling sessions), self-caring (3 home-delivered video tapes and journals), combined caring (1 nurse counseling session plus 3 videotapes and journals) and no intervention (control) on the emotional healing, integration of loss and couple well-being of women and their partners (husbands or male mates) in the first year after miscarrying.

**Technical Approach:** 340 couples(or 680 individuals) will be recruited to participate in a 4 group, pre-test, post-test randomized study of a counseling intervention meant to reduce distress and enhance couple well-being following miscarriage. Upon recruitment, individuals will be informed that they may be randomized into a group that will not receive any treatment. Four groups will be followed for 1 year. All participants will fill out 4 questionnaire packets throughout the study period. The first will be mailed after the couple initially agrees to participate. The other questionnaire booklets will be sent at 6 weeks, 16 weeks and 1 year after their initial enrollment in the study.

**Progress:** The study reached its targeted enrollment of 340 couples during FY05. Thus far, 183 couples have completed the entire study protocol. Steady progress is being made towards achievement of study aims. Preliminary data analyses have begun. The intervention nurses are conducting in-home counseling sessions with couples and meet regularly for supervision. Study data are being double entered into an SPSS secure database. Syntax files for data analysis have been developed. Data Safety and Monitoring Board meetings occur at the University of Washington as mandated by the funding source. Recruitment is closed at all sites: University of Washington Medical Center, Madigan Army Medical Center, Group Health Cooperative, and Evergreen Hospital Medical Center.

During FY06, recruitment was reported as completed and all participants completed the interventions. Data cleaning and data analysis continues

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205037	<b>Status:</b> Ongoing
<b>Title:</b> Determining the Effectiveness of a Stroke Prevention Program		
<b>Principal Investigator:</b> Lori A. Loan, RNC, Ph.D.		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Mona O. Bingham, AN; LTC Jon C. Allison, MC; Nancy A. Cox, RN, BSN; Samuel C. Sorbello, RN		
<b>Start - Completion:</b> 2/3/2005 - Jan 2011	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/20/2006

**Study Objective:** To determine the effectiveness of an intensive one-on-one case management program designed to control identified risk factors for stroke and reduce the incidence of stroke in target population.

**Technical Approach:** This longitudinal study will use a randomized, two group repeated measures design to compare a nurse case management stroke prevention program to standard care provided by primary care services in order to determine the effectiveness of an intensive 1:1 case management intervention. After one year there may be a cross-over group of those control subjects who wish to enter the case management intervention program. The study's primary outcomes are blood pressure, LDL, HgA1c, and BMI (as calculated from measures of height and weight). Secondary outcome measures include including incidence of vascular events, hospitalizations, emergency room visits, progression of carotid artery disease, control of atrial fibrillation, tobacco cessation and decreased tobacco use, and exercise level. Quality of life, mental wellness, and overall health will also be measured through approved survey instruments available on the MAMC web system.

Medical information from case management visits, medical records, hospital information, and health instruments will be used to compile data for this study. Chi-square, t-tests, ANOVA with repeated measures, and Mann-Whitney U tests will be used to compare group outcomes. The actual 1:1 case management intervention will last one year. At the end of one year, each patient will be re-evaluated to determine if case management services are still needed. At this time, control patients will be asked if they would like to receive case management services until capacity is reached for case management load. Results will be analyzed at 6 months, 1 year, and for 5 years there after for study subjects.

**Progress:** This protocol remains ongoing. All baseline and six month data collection is complete. One year data has been collected for over half of the participants.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204084	<b>Status:</b> Ongoing
<b>Title:</b> Impact of Inpatient Physician Order Entry on Medication Administration and Dispensing Error Rates in the Neonatal Intensive and Intermediate Care Units		
<b>Principal Investigator:</b> Lori A. Loan, RNC, Ph.D.		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Donna C. Whitney, MC; James A. Taylor, M.D.; Susan Blackburn, Ph.D., RNC		
<b>Start - Completion:</b> 6/14/2004 - Jun 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/20/2006

**Study Objective:** The proposed study will be conducted in two phases. Phase One is designed to pilot test an observational methodology called Line Operator Safety Audit (LOSA) and modify LOSA for use with medication error detection in the NICU/ICN and inpatient pharmacy. Phase One will also include refinement of data collection instruments and techniques. Once the optimal observation techniques and data collection instruments are determined, Phase Two will begin. In this phase the number and types of observed medication administration and dispensing errors will be compared before and after inpatient physician order entry is initiated in the NICU/ICN at Madigan Army Medical Center.

**Technical Approach:** This study will examine medication errors before and after the initiation of inpatient physician order entry (IPOE) in the Neonatal Intensive Care Unit (NICU) or Intermediate Care Nursery (ICN), and point out what types of errors are common in this patient population. Approximately 25 health care personnel dispensing (pharmacy personnel) or administering (nursing personnel) medications for NICU or ICN patients will be watched until approximately 750 opportunities-for-error have been observed. The study will use a pretest-posttest design and appropriate statistical techniques (t-test, Mann Whitney U or chi-square) to compare medication administration and dispensing error rates from two data collection periods- 1-month before NICU/ICN IPOE begins and 4 months after NICU/ICN IPOE is initiated. Information from the study will be used to develop practical error-prevention strategies.

**Progress:** All medication variance observations have been completed. In total, there were 253 baseline and 266 post physician order entry observations. Preliminary analysis suggests a statistically significant decrease in the overall medication administration variance. The protocol remains ongoing to complete data analysis already in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 204031		<b>Status:</b> Ongoing	
<b>Title:</b> Military Nursing Outcomes Database: Analysis & Expansion (MilNOD IV)					
<b>Principal Investigator:</b> Lori A. Loan, RNC, Ph.D.					
<b>Department:</b> Nursing				<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Patricia A. Patrician, AN; COL Laura R. Brosch, AN					
<b>Start - Completion:</b> 4/8/2004 - Aug 2005		<b>Funding:</b> Triservice Nursing Research Program via The Geneva Foundation		<b>Periodic Review:</b> 12/13/2006	

**Study Objective:** This is the fourth study (MilNOD IV) in a program of research examining nurse staffing and patient outcomes. This particular study will shift from database development to examining aspects of structure, process, & outcome.

**Technical Approach:** Data deemed valid and reliable from the study, "Establishing a Military Nursing Outcome Database" (Brosch, 2002), will undergo secondary analyses to examine relationships between nursing structure indicators, and patient and nurse outcome indicators. The research team will specify a series of regression models, examining each outcome variable separately. For survey subscales on the Nursing Work Index-Revised and the Patient Satisfaction Survey, correlations will be performed to examine associations among independent variables and between independent and dependent variables. Simple Pearson's correlations will indicate whether a relationship exists between nurse and patient satisfaction.

**Progress:** Subjects include patients who were surveyed for the patient satisfaction indicator and nursing personnel surveyed for their education/experience/certification activities, their job satisfaction, and the attributes of their work environment. Retrospective data are collected from patients participating in the pressure ulcer prevalence survey as well. Each type of survey was conducted at MAMC once in FY'06, except the pressure ulcer prevalence data are collected biannually. All 13 participating MTFs submitted survey data along with shift-level nurse staffing data and patient outcome data to a project-specific electronic database during FY '06. Data collection has now been discontinued and a data analysis plan is being formulated.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201104	<b>Status:</b> Ongoing
<b>Title:</b> Newborn Infant Speech Perception		
<b>Principal Investigator:</b> Lori A. Loan, RNC, Ph.D.		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Randall C. Zernzach, MC, USAF; Tricia K. Grannis, R.N.; Christine Moon, PhD		
<b>Start - Completion:</b> 11/1/0168 - May 2003	<b>Funding:</b> UW	<b>Periodic Review:</b> 6/20/2006

**Study Objective:** Characterize the effect of experience on typically developing newborn infants' perception of speech and language.

**Technical Approach:** The current proposal for research is for a 2-year study of newborn infant discrimination of familiar and unfamiliar speech sounds. Three experiments will comprise the study. The first will test newborns' ability to discriminate mother's voice from a stranger voice when the speech samples are brief. The second experiment will examine whether infants respond preferentially to their mother's native language when the samples are brief. In the third experiment, infants will be tested for their ability to discriminate brief vowel sounds from among well- and poorly-formed exemplars in English. Each of the three experiments will require data from 80 participants for a total of 240 infants. Because the attrition rate for completion of the 10-minute session is likely to be about 35%, it is expected that approximately 360 infants will be recruited and that 120 will not complete the experiment.

Prospective participants will be 1-5 days old and will be identified from hospital records. Eligibility will be based upon criteria that indicate typical, uncomplicated newborn development. Parents will be contacted in their hospital rooms by the experimenters who will present the study and obtain signed, informed consent. Infants will be transported to a quiet area near the newborn unit for a 20-minute session. A pacifier that is connected to a pressure transducer will be placed in the infant's mouth. If the pacifier is accepted, headphones will be placed over the infant's ears. After a 1-minute baseline period to measure sucking pressure, computer-controlled sounds at conversational levels of intensity will be presented for 9 minutes, contingent upon infant sucking pressure. Frequency of sucks during particular stimuli will be the dependent measure. Data analysis will be based upon a comparison of sucking frequency during different sounds. Results of the experiments will be presented at professional conferences and submitted as articles for publication in professional journals.

**Progress:** Due to an unexpected loss of research funding, the pace of data collection slowed during the past year; however, analysis of data in the database continued. The analyses confirm newborn recognition and preference for mother's voice, and they extend past results by demonstrating that pitch of the voice (fundamental frequency and/or spectral slope) is an important cue to voice recognition by newborn infants. This is consistent with the idea that newborns are relying on prenatal voice cues for postnatal perception. Pending replication of the pitch results, a paper on the topic will be submitted to an infant development journal.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202075	<b>Status:</b> Ongoing
<b>Title:</b> Secondary Analysis of NICU Modified Care Environment Projects		
<b>Principal Investigator:</b> Lori A. Loan, RNC, Ph.D.		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Karen A. Thomas, Ph.D., RN; Susan T. Blackburn, Ph.D., RN, FAAN; Shu-Yuann Wang, MS, RN; Ms Sara Brown, RN; Shao-Yu Tsai		
<b>Start - Completion:</b> 1/7/0168 - May 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/9/2006

**Study Objective:** Secondary analysis of data collected in previously approved projects is proposed. Prior human use approvals were (1) The Effects of a Modified Care Environment on the Growth and Development of High Risk Infants, P.I. LTC Michelle T. Renaud, approved 4 September 1992, and (2) a continuation and extension, Neonatal Outcomes in a Modified NICU Environment, P.I. LTC Michelle T. Renaud, approved 13 July 1993. Additionally these projects were approved by the University Of Washington Human Subjects Division. Both projects included Karen Thomas and Susan Blackburn, UW faculty, as Co-Principal Investigators.

The original projects involved comparison of two neonatal intensive care unit environments that included reduced light and sound levels. Infants randomized to the control group remained in the standard nursery. Both groups of infants received standard medical and nursing care in all respects, except for the nursery environment. Data collect during the study included infant health status, parent demographic information, duration of hospitalization, environmental sound and light levels, neurologic and behavioral assessment and infant sleep-wake states. Infant sleep-wake stated was measured by 3-4 hour video recordings performed at 34 weeks gestational age and again at time of discharge. Video recordings were performed while infants were in incubators or in open crib and display the infant's body and face.

For the second analysis, investigators are requesting permission for activities: (1) Photo copies to be made of existing video coding sheets, (2) Access to video tapes for recording purposes, (3) Use of existing data base by the three graduates named above.

**Technical Approach:** The proposed research is a secondary analysis of data from a previously approved project that was conducted at MAMC in conjunction with nurse researchers from the University of Washington Department of Family and Child Nursing. Permission is requested for use of data by a total of three nursing graduate students. Computer files containing the data from the original project, excluding identifiers, is currently in the possession of Karen Thomas. Permission is requested to photocopy the video coding sheets, currently held at MAMC for use by investigators at the University of Washington. Permission is also requested for temporary use of the videotapes at the U.W. The video coding sheets will be used to enter the raw data into a computer file. Videos will be used to determine reliability of original coding and to code additional infant behaviors and care giving activities.

**Progress:** One doctoral student, Shu-Yuann Wang, continues to analyze data from the parent project. This data is anonymized; investigators at the University of Washington do not have access to the original code list, and the data set does not include any information which would allow identification of subjects. Ms. Wang will complete her dissertation by June 2006. Two graduates, Shao-Yu Tsai and Sara Brown, whose Masters theses were based on the secondary analysis, along with Dr. Karen Thomas, have submitted a journal manuscript based on study findings. Ms. Tsai's poster presentation at the Western Institute for Nursing conference (An Exploratory Analysis:

Environmental Modifications on the Sleep-Wake State in Preterm Infants - Portland, OR, 2004)  
received an award for doctoral student research.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206108	<b>Status:</b> Ongoing
<b>Title:</b> Army Nurse Corps Officers' Deployment Experiences and Reintegration		
<b>Principal Investigator:</b> COL Laurie A. McNabb, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, Ph.D.; LTC Denise Hopkins-Chadwick, AN; Mary S. McCarthy, RN, PhD		
<b>Start - Completion:</b> 7/10/2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To explore the many factors that impact nurses' ability to perform their jobs during all phases of a deployment; prior to the deployment, during the deployment, and during the post-deployment phase. Outcomes of this study will serve as the basis for the development of the best strategies to support nurses prior to and following a deployment in order to facilitate the smoothest transition, between workplaces.

**Technical Approach:** Prospective Data Collection Procedures: Army Nurse Corps Officers will be recruited based on the inclusion criteria and availability. Nurses interested in participating in the study will be contacted by phone or email. During this initial call, one of the study investigators will discuss a variety of issues with each participant such as the study purpose, what will be needed from them as participants, who will be at the group or interview, and other specifics of the focus group sessions. They will be given information about the study and their questions will be answered. Those volunteering to participate will be scheduled for attendance at focus group sessions or interviews through telephone calls or personal interactions carried out 7 to 14 days prior to the session. To increase attendance, participants will again be contacted telephonically by a research team member 24 hours prior to the date and time of the session (Goldstein & McDonald, 1987; Krueger, 1988; Stewart & Shamdasani, 1990). Participants will also be given a demographic data collection sheet and asked to complete it and bring it to the focus group meeting. These sheets will be collected from participants after consenting is complete. If participants fail to bring the sheet, they will be asked to supply demographic information at the time of the focus group session.

**Progress:** This protocol remains open to enrollment. Twelve subjects have participated in focus groups at MAMC so far.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206107	<b>Status:</b> Ongoing
<b>Title:</b> Menstruation During Deployment: Women's Attitudes Towards Menstrual Suppression		
<b>Principal Investigator:</b> LTC Lori L. Trego, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, Ph.D.; LTC Denise Hopkins-Chadwick, AN; 1LT Sandra L. Gordy, AN		
<b>Start - Completion:</b> 7/10/2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objective is to perform instrument development and testing of a military-specific measure of the experience of menstruation and associated attitudes towards menstrual suppression in a deployed environment. Specific Aims are to (1) establish the reliability (internal consistency) of an instrument that measures military women's experiences of menstruation and attitudes towards menstrual suppression and (2) establish the validity (content, face, construct, convergent, discriminant) of an instrument that measures military women's experiences of menstruation and attitudes towards menstrual suppression.

**Technical Approach:** Data collection will be the administration of a paper and pencil survey consisting of the Military Women's Attitudes Towards Menstrual Suppression, the Attitudes Towards Menstrual Suppression Scale (ATMS), the Menstrual Attitudes Questionnaire (MAQ), and a Deployed Menstrual Health Practice Questionnaire (DMHPQ). Targeted sample size per power analysis is 300-500 participants, as required for factor analysis. Psychometric testing with this sample size allows for tests of internal consistency and item evaluation in the assessment of reliability as well as exploratory factor analysis for construct validation. Several methods of construct validity have been chosen for this study: content validity, face validity, construct validity, and convergent and discriminant construct validity. The sample will therefore complete a questionnaire that consists of the MWATMS, as well as two other valid instruments that will be used to test convergent and discriminant validity: the Menstrual Attitude Questionnaire (MAQ) and the Attitudes Towards Menstrual Suppression scale (ATMS).

**Progress:** Twenty-three Soldiers have participated in this study. There have been no adverse occurrences and no preliminary findings are available. Enrollment will continue during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206002	<b>Status:</b> Completed
<b>Title:</b> Military Women's Thoughts about Menstruation and Menstrual Suppression During Deployment		
<b>Principal Investigator:</b> LTC Lori L. Trego, AN		
<b>Department:</b> Nursing	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, Ph.D.		
<b>Start - Completion:</b> 10/14/2005 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** This study will be conducted in two phases. The purpose of Phase 1 is to describe menstrual experiences of women who have been deployed to a military theater of operations and to explore their experiences with menstrual suppression. Phase 1 research questions are: (1) How do military women manage menses while deployed? (2) How do military women feel about using continuous oral contraceptives for suppression of menses while they are deployed?

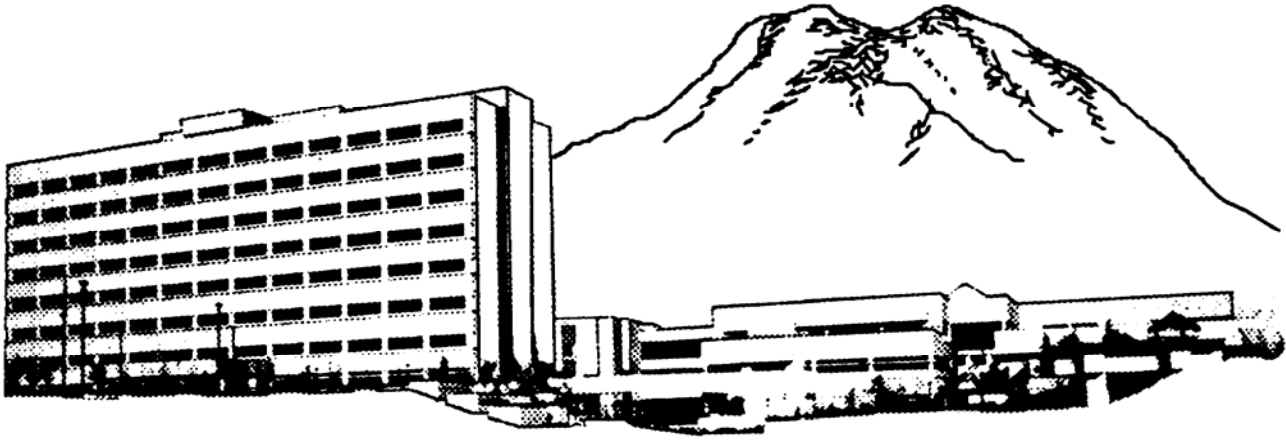
The purpose of Phase 2, pilot instrument development and testing, is to generate an instrument that measures military women's attitudes towards menstruation and menstrual suppression. Phase 2 research questions are: (1) What are the initial psychometric properties of the instrument? (2) To what extent is further use of the instrument feasible?

**Technical Approach:** Phase 1, Interviews: A qualitative descriptive approach will be utilized to explore attitudes towards menstruation and menstrual suppression among military women who have returned from a deployment to a theater of military operations. The projected sample size is 30 women, or until themes become repetitive. Data Collection: Sampling will occur at the Fort Lewis SRP site. Subjects will participate in a focused interview utilizing open-ended questions which have been derived from a review of literature. Questions will be focused on the experiences of menstruation and suppression of menstruation using continuous oral contraceptives while in a deployed environment. The interviews will be limited to 30 minutes, being cognizant of the time constraints on these women's lives. The interviews will be conducted in a private area within the SRP site. The data will be audio tape recorded and transcribed verbatim by either a qualified transcriptionist or the PI. Data Analysis: Inductive content analysis will be conducted to determine themes which describe the menstrual experiences and suppression of menses, as it is applicable, of deployed women.

Phase 2, Instrument development: The Phase 1 themes will be utilized in the construction of a military-specific tool to measure military women's menstrual attitudes and their attitudes towards menstrual suppression during deployment. Items for the measure will be generated based on themes from the interviews. A women's health expert panel, will be consulted during item generation. Content validity will be determined by both the women's health expert panel and a lay panel, which will consist of military women. Revisions to the instrument will be made based on content validity assessments. The expert panel will again be consulted. The final step of instrument development is a pilot test of the instrument on 50-60 women. The sample will be from the SRP site. Recruitment will occur in the same manner as with the interviews. The instrument will be administered in a private area of the SRP. A face validity assessment will be included with the instrument for the pilot subjects to complete. The pilot data will be analyzed for reliability and feasibility. Based on the results of the pilot data, the instrument will be revised and ready for future study. The future study would determine the instrument's validity and reliability.



**Progress:** Phase 2, "Instrument Development," has been conducted. Based on the results of Phase 1, the instrument, "Military Women's Attitudes Towards Menstrual Suppression" was revised and pilot tested according to protocol procedures. Data analysis was performed according to protocol and the instrument was found to have sufficient reliability and validity for future study. Refer to protocol #206107 for next study in the development of this instrument. This protocol was reported as completed during FY 2006.



## **Detail Summary Sheets**

Anesthesia Students, Department of Nursing

### Detail Summary Sheet

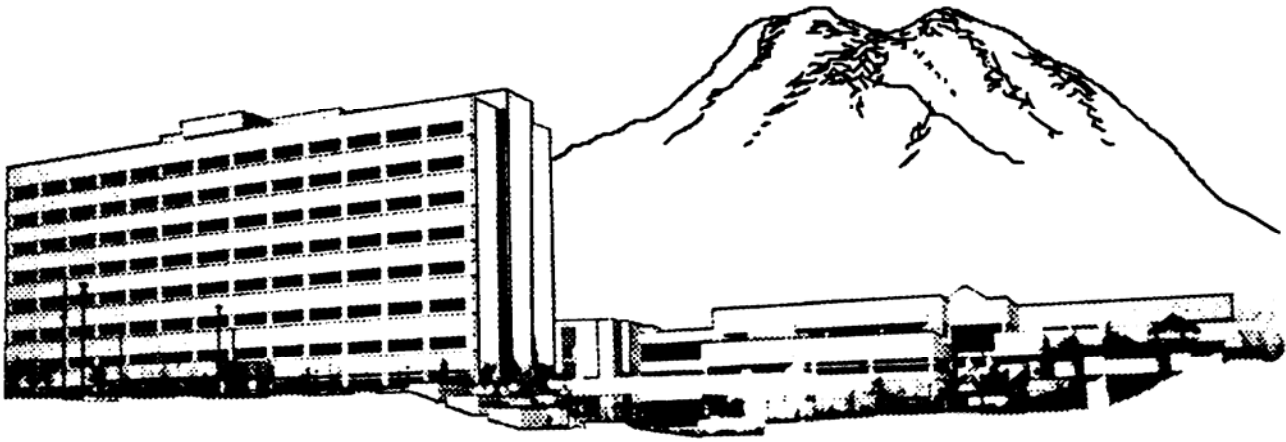
<b>Date:</b> 30 Sep 06	<b>Number:</b> 204112	<b>Status:</b> Completed
<b>Title:</b> Efficacy of Preoperative Valerian (Night Before) on Day of Surgery Anxiety		
<b>Principal Investigator:</b> CPT Mary K. Hannon, AN		
<b>Department:</b> Nursing/Anesthesia	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Angela M. Downs, AN; Mark D. Hachey, CRNA		
<b>Start - Completion:</b> 11/5/2004 - Oct 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/23/2005

**Study Objective:** To determine if valerian reduces anxiety in patients undergoing general or regional anesthesia when administered the night before surgery.

**Technical Approach:** Recruitment: Identification of potential candidates for participation in the study will be accomplished by prescreening of the surgical roster, and identified candidates recruited during the pre-anesthesia interview. CPT Angela Downs or CPT Mary Kate Hannon will complete consent after the pre-anesthesia interview. Informed consent will be obtained prior to the administration of any of the anxiety measuring instruments (VAS/SAI). Upon collection of demographic data, a standardized direction and information statement will be read to each participant. Once the participant verbalizes understanding of the process, the SAI and VAS in relation to anxiety of the upcoming surgery will be administered. The principle or associate investigators will be present in the room for this process to answer any questions, and to collect and secure the data. Randomization of test subjects will be accomplished by pre-prepared chart calculated by Mr. Troy Patience of the Department of Clinical Investigations, MAMC using Microsoft Excel. Patients will receive either placebo, or 800mg active valerian according to the randomization chart. Each day investigators will sign out approximately 15 doses of the pre-numbered standard plastic prescription vials containing the valerian or placebo. Distribution will be accomplished by the investigators during the preoperative interview. An instruction sheet explaining possible side effects of this medication will be provided to the subjects, as well as instructions if a suspected allergic reaction or acute side effects occur. The time frame of actual administration will be approximately 2200 hrs the night before surgery, or at the hour of sleep, in accordance with other surgical restrictions, i.e., NPO after midnight.

Re-evaluation of test subjects: Participants will be asked to repeat both the VAS and SAI forms while in the preoperative holding area and prior to the insertion of IV catheter(s) or any other surgical adjunct. Either investigator will again collect the VAS and SAI form data assuring consistency and confidentiality. Outcome variables are the level of anxiety that will be measured using the STAI-S questionnaire and VAS, with an anticipated reduction in the level of anxiety in individuals taking the 800mg valerian versus the placebo. Differences between groups will be determined by a statistical analysis of the SAI and the VAS scores separately using Analysis of Covariance.

**Progress:** This protocol was reported as completed in October 2005, with 143 subjects enrolled. **Findings:** Under the conditions of this study, there were no significant differences between the pre and post SAI and VAS for either the placebo or valerian group. Serendipitously, the investigators found a significant difference in preoperative anxiety between males and females. Postulated reasons there was no significant difference (1) valerian has no efficacy, (2) timing of dose administration and post test, (3) dose of valerian administered, (4) single dose versus multiple doses, and (5) influence of gender roles on anxiety.



## **Detail Summary Sheets**

Department of Obstetrics/Gynecology

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206042	<b>Status:</b> Completed
<b>Title:</b> Resident Training in Assessment of the Sexual Assault Patient Utilizing Simulation		
<b>Principal Investigator:</b> CPT Anne C. Burris, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Shad H. Deering, MC; LTC Michael K. Chinn, MC		
<b>Start - Completion:</b> 1/6/2006 - Jan 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective is to evaluate the use of a simulation-based training program on resident comfort with and understanding of evaluation of a sexually assaulted patient.

**Technical Approach:** This study plans to utilize the NOELLE childbirth simulator module at the Anderson Simulation Center to both evaluate resident performance of the evaluation of a sexual assault patient as well as investigate their comfort level with the procedure. This evaluation is to be done before and after simulation testing to see if this is a helpful model that should be incorporated into our standard simulation curriculum.

**Progress:** Results: After training, residents reported that they had a better understanding of the procedure for the examination, what medications should be given for STD prophylaxis, what anatomic findings must be recorded, and the chain of custody that must be maintained.

**Conclusions:** A simulation-based course can improve resident confidence with the performance of the examination of a sexual assault patient. This training is especially important in the explanation of the requirements for the collection of evidence.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205140	<b>Status:</b> Ongoing
<b>Title:</b> Continuous Use of the Oral Contraceptive for Menstrual Cycle Suppression and the Effects on Bone Density; a Prospective, Randomized, Clinical Trial		
<b>Principal Investigator:</b> LTC Michael K. Chinn, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Leslie Miller, M.D.; LTC Antonio G. Balingit, MC; Nancy A. Poffenberger, PAC, Ph; COL Diane M. Flynn, MC; LTC Wendy Ma, MC; LTC Jeffery L. Clemons, MC; COL Jon A. Proctor, MC; Gregory E. Chow, MD; CPT Tammy J. Mantzouris, MC; CPT Andrew E. Fong, MC		
<b>Start - Completion:</b> 1/13/2006 - Dec 2011	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/19/2006

**Study Objective:** To identify the dose of ethinyl estradiol (EE) in combination with levonorgestrel (LNG) or norethindrone acetate (NETA) that, when taken daily, results in rapid and sustained amenorrhea over two years with minimal changes in bone density.

**Technical Approach:** This study looks at what pill dose, when taken every day, will work the fastest to stop all period bleeding and which dose will keep the bleeding away for two years of daily use. Women will provide a monthly report of pill use and bleeding and have their bone density measured at baseline and after two years to see if the two estrogen doses or two progestin types will vary these and other safety effects. In addition, women stopping the study drug will be followed until menstruation returns to document reversibility. Female soldiers need to know which dose of birth control pill can induce menstrual cycle suppression, the safety of taking these pills every day for up to 2 years, the effects of an induced amenorrhea on their bone density, and the time it takes for menses to return following suppression.

**Progress:** Initiation of this protocol is pending funding. An amendment was submitted due to an offer of fewer funds than requested. The study has changed from a four arm to a two arm trial looking at the lower estrogen doses. Enrollment was dropped from 720 to 360, and length of subject involvement shortened from 24 to 18 months. The study also would no longer be providing menstrual hygiene products to subjects or be able to hire a study provider (ARNP); just a dedicated research coordinator.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 81035	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0041: Surgical Staging of Ovarian Carcinoma		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 1/16/1981 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatments protocols; to determine the complication rate of the procedures.

**Technical Approach:** This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a complete and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

**Progress:** This protocol closed to patient entry in February 1987, with thirteen patients enrolled. Three patients remain disease free and continued to be followed at MAMC during FY06. Final analysis of this trial appears in the January 1988 GOG Statistical Report. The manuscript derived from this trial was published in Surg. Gynecol. Obstet 1989.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 81105	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0052: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage II Ovarian Adenocarcinoma		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 8/21/1981 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG 0025.

**Technical Approach:** Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

**Progress:** This protocol closed to patient entry in July 1985, with six patients enrolled. One patient remains disease free and continued to be followed at MAMC during FY06. Final analysis of the study appears in the July 1988 GOG statistical report. Seven abstracts and publications (listed in the GOG statistical report) evolved from this clinical trial.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 84033	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0072: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 2/17/1984 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

**Technical Approach:** Patients without prior chemotherapy of radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for five years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cisplatin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cisplatin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

**Progress:** This protocol closed to patient entry in February 1992, with ten patients enrolled. Five patients continued to be followed at MAMC during FY06, three patients have been lost to follow-up and two patients with no evidence of disease continue to be followed out-of-state. Statistical analysis appears in the July 2002 GOG Statistical Report. Manuscript derived from this trial was published in JCO 1995.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 84074	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0078: Evaluation of Adjuvant VP-16, Bleomycin, and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 8/17/1984 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan. 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

**Technical Approach:** Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be eligible a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted. Per addendum of Jan. 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

**Progress:** This protocol closed to patient entry in February 1992, with one patient enrolled who remains disease-free with a last follow-up (out-of-state) in FY02. Final analysis of this study appears in the July 1993 GOG Statistical Report. Manuscripts derived from this clinical trial had been published in 1994.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 86089	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0085: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjuvant to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-Aortic Nodes		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 9/19/1986 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.

**Technical Approach:** Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years.

**Progress:** This protocol closed to patient entry in December 1990, with two patients were enrolled. One patient was lost to follow-up (last seen at MAMC in 1985). The second patient has been disease free and continued to be followed at MAMC during FY06. Final statistical analysis appears in the July 1997 GOG Statistical Report. Two abstracts and a publication (listed in the GOG statistical report) have been derived from this clinical trial.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 87104	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0092: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy versus No Further Therapy		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 8/21/1987 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To determine the value of adjunctive pelvic radiation in the treatment of Stage 1B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

**Technical Approach:** All patients with Stage 1B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

**Progress:** This protocol closed to patient entry in December 1995, with one patient enrolled in FY 1988, who remains disease free and continued to be followed at MAMC during FY06. Final analysis appears in the January 1999 GOG Statistical Report. An abstract and publication have been derived from this clinical trial.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 87028	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0095: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected IAI and IBI and IAII and IBII Ovarian Cancer, Phase III		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 11/21/1986 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAI and IBI patients with poorly differentiated tumors and stage IAII and IBII (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

**Technical Approach:** The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin in patients with ovarian cancer. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion. Chemotherapy will consist of cyclophosphamide, 1 mg/m<sup>2</sup> I.V., on day 1 plus cisplatin, 100 mg/m<sup>2</sup> IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

**Progress:** This protocol closed to patient entry in March 1994, with five patients enrolled. One patient remains disease free and continued to be followed at MAMC during FY06. Final analysis of this trial appears in the July 2000 GOG Statistical Report. Abstracts and manuscripts derived from this trial have been published as listed in the GOG Statistical Report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 87091	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0099: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 7/17/1987 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

**Technical Approach:** Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGy in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

**Progress:** This protocol closed to patient entry in July 1995, with three patients enrolled. All are clinically disease free and continued to be followed during FY06. Final analysis appears in the January 1999 GOG Statistical Report. Two abstracts were published. Manuscript derived from this clinical trial is under revision for publication.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 93063	<b>Status:</b> Ongoing
<b>Title:</b> GOG 0123: A Randomized Comparison of Radiation Therapy & Adjuvant Hysterectomy vs Radiation Therapy & Weekly Cisplatin & Adjuvant Hysterectomy in Patients with Bulky Stage IB Carcinoma of the Cervix		
<b>Principal Investigator:</b> LTC Louis A. Dainty, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jane Shen-Gunther, MC		
<b>Start - Completion:</b> 5/6/1994 - Indef	<b>Funding:</b> GOG	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To evaluate the addition of weekly chemotherapy with Cisplatin during radiation therapy in patients with bulky Stage IB carcinoma of the cervix.

**Technical Approach:** This study randomizes patients to two different treatment regimens. Both regimens include radiation therapy followed by hysterectomy. Regimen I - Radiation Therapy Plus Adjuvant Hysterectomy - Patients will undergo combined external and intracavitary radiation therapy followed by extrafascial hysterectomy (total doses of 13000 cGy). Regimen II - Radiation Therapy Plus Weekly Cisplatin Infusion Plus Extrafascial Hysterectomy. Patient will undergo radiation therapy to receive a total dose of 13000 cGy using a combination of external and intracavitary radiation therapy. Each week during external radiation therapy and during the intracavitary applications the patient will receive an infusion of cisplatin 40 mg/m<sup>2</sup> not to exceed 70 mg maximum in any single infusion, up to a maximum of 6 doses of cisplatin. Extrafascial hysterectomy will be carried out no later than six weeks following the last day of treatment in both regimens.

The principal parameters to determine the efficacy of weekly cisplatin during radiotherapy are: 1) Outcome variables (recurrence-free interval (RF), survival and local control rate); 2) Tumor characteristics; 3) Host characteristics; 4) Adverse effects; 5) Therapy administered.

**Progress:** This protocol closed to patient entry in April 1997, with one patient enrolled who remains disease free and continued to be followed during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206029	<b>Status:</b> Ongoing
<b>Title:</b> Simulation Training for Postpartum Hemorrhage		
<b>Principal Investigator:</b> MAJ Shad H. Deering, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 12/14/2005 - Jan 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To have OB/GYN residents perform a simulated postpartum hemorrhage scenario to evaluate their clinical management skills and evaluate a standardized grading form.

**Technical Approach:** A standard postpartum hemorrhage simulation has been designed using the NOELLE mannequin and the new uterine hemorrhage model at the Anderson Simulation Center (designated for use by OB/GYN). Standardized objective and subjective evaluation sheets have been created to evaluate resident's performance. Prior to beginning the simulation, residents will be given a case scenario describing the patient's clinical situation. Residents will enter the room and address the active bleeding that is occurring. All simulations will be digitally recorded with at least two evaluators present to assess the resident's performance using the standard evaluation forms. Residents will be able to perform an examination and ask for medications to be administered. An empty syringe will be used by a staff member playing the part of the nurse to "administer" any medications requested and the resident will be made to clarify the dose and route of the medication. The simulation will end when the resident has performed an appropriate physical examination, fundal massage, and administered two medications in the correct dose and route, or when a total of 5 minutes has expired. After the simulation, the resident will be shown their grading scores and additional instruction will be performed in any areas that were deficient.

**Progress:** This protocol remains ongoing with fourteen residents from MAMC who took part in this study during FY06. All fourteen completed the simulation training protocol and data analysis is currently being conducted.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206098	<b>Status:</b> Ongoing
<b>Title:</b> Serum Estradiol Levels in Patients with Polycystic Ovarian Syndrome undergoing Ovulation Induction with Clomiphene Citrate		
<b>Principal Investigator:</b> CPT Shannon K. Flood, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Jon A. Proctor, MC		
<b>Start - Completion:</b> 6/5/2006 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To correlate serum estradiol levels and ovulation rates in patients with polycystic ovarian syndrome undergoing ovulation induction with clomiphene citrate.

**Technical Approach:** This is a prospective observational study to analyze the relationship between serum estradiol levels and ovulation rates in women with polycystic ovarian syndrome undergoing ovulation induction with clomiphene citrate. Women enrolled in the study will take 50-250 mg of clomiphene citrate on days 3-7 or days 5-9 of their menstrual cycle. They will also present for transvaginal ultrasound and a serum estradiol levels on menstrual cycle day 12, 13, or 14. Patients will be provided with urinary lutenizing hormone detection kits, and will be instructed to record the day of their LH surge. Lastly, patients will obtain a serum progesterone concentration seven days after their LH surge. This data will be organized in a spreadsheet format. The study participants will then be divided into two groups, those who ovulated and those who did not. Mean estradiol levels will then be calculated for each group. Appropriate post hoc statistical analysis will then be performed to evaluate for any correlation between estradiol levels and ovulation rates.

**Progress:** A total of 4 patients have enrolled in the study at MAMC during FY06. The study has been temporarily on hold with COL Proctor's retirement this summer, and I myself (the PI) have been on an off service rotation and have been unable to consent patients. However, I plan on adding the REI specialist, COL Chow, to the protocol and starting enrolling new patients shortly.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 99077	<b>Status:</b> Completed
<b>Title:</b> Misoprostol for the Medical Management of Non-viable First Trimester Pregnancies		
<b>Principal Investigator:</b> CPT Jasmine J. Han, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Peter E. Nielsen, MC; Troy H. Patience, B.S.; COL Milo L. Hibbert, MC; MAJ Jason D. Parker, MC; CPT Robert G. Fowers, MC; LTC Louis A. Dainty, MC		
<b>Start - Completion:</b> 3/9/2000 - Mar 2001	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/20/2006

**Study Objective:** The purpose of this study is to examine the effectiveness of Misoprostol (Cytotec; GD Searle and Co., Chicago, IL) for the management of non-viable first trimester pregnancies. Specifically, Misoprostol (15-S-15-methyl PGE1) will be compared to a placebo with expectant management in who have documented non-viable gestations. We will examine the following outcome variables: time to resolution, number of patients requiring dilation and curettage, change in hematocrit, cost to the institution, patient satisfaction, and reported side effects.

**Technical Approach:** Patients presenting to the OB/GYN clinic with a nonviable gestation, diagnosis documented by endovaginal ultrasound will be enrolled. Ultrasonic findings will be verified by two of the resident staff from the obstetrics and gynecology department of Madigan Army Medical Center. Patients consenting will be directed to the OB/GYN clinic for evaluation, exam, and counseling and to watch the video giving explanation of purpose of the study and the planned procedure, but also expected side effects and possible complications. Patients will be randomized into two groups: study group receiving Misoprostol per vagina and the control group receiving a placebo per vagina. Subjects will be issued an envelope and go to the pharmacy to pick up their study medication, blinded to them and the provider. They will also be given Motrin and Phenergan to help alleviate undesired side effects. Four 200 ug tablets of Misoprostol or placebo will be placed in the posterior fornix of the vagina using a speculum under the direct visualization of the provider. Patients will return in 24 hours for re-examination. If no evidence of an intrauterine pregnancy remains, patients will be informed that their miscarriage was complete, given precautions and asked to make an appointment for follow-up in 4 weeks in addition to weekly visits to the lab for quantitative BHCG. All patients will be followed until the quantitative BHCG has fallen zero to ensure resolution of the pregnancy event.

Patients with evidence of a gestational sac will be given a second dose of Misoprostol or a D&C if they choose to withdraw from the study or a surgical intervention if it is deemed clinically indicated by the attending staff. Again, subjects will be given appropriate counseling and precautions and asked to follow up in an additional 24 hours for re-evaluation. Surveys will be given at each visit and follow up to evaluate patient satisfaction and also to query for unintended side effects and complications.

**Progress:** This protocol completed enrollment during FY06, with thirty patients enrolled, five during the last 12 months. Data analysis has been conducted and results scheduled for presentation at an upcoming AFD meeting in October 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204111	<b>Status:</b> Ongoing
<b>Title:</b> Glyburide Compared to Insulin in the Management of White's Classification A2 Gestational Diabetes		
<b>Principal Investigator:</b> MAJ Demetrice L. Hill, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrea D. Shields, MC; LTC Damian J. Paonessa, MC, USAF; MAJ Jennifer L. Gotkin, MC; LTC Bobby C. Howard, MC, USAF; LTC Peter G. Napolitano, MC; COL Peter E. Nielsen, MC; CPT Shannon K. Flood, MC		
<b>Start - Completion:</b> 12/14/2004 - Mar 2006	<b>Funding:</b> Tripler AMC via MIPR	<b>Periodic Review:</b> 8/22/2005

**Study Objective:** Pregnant women who meet the diagnostic criteria for gestational diabetes and fail dietary control will be randomized into two groups. One group will be prescribed glyburide and the other insulin in order to achieve optimal glucose control in pregnancy as manifested by decreased incidence of large for gestational age fetuses.

**Technical Approach:** This study will randomize 100 pregnant women into two groups, Group 1 will be prescribed glyburide and Group 2 will be prescribed insulin in order to achieve optimal glucose control in pregnancy as manifested by decreased incidence of large for gestational age fetuses. Subjects randomized into standard therapy insulin arm will have their insulin dose calculated by established standards. Insulin will be adjusted on a weekly basis in order to maintain optimal glucose control. Women assigned to receive glyburide will begin with 2.5 mg orally with the morning meal. Glyburide dosage will be increased weekly as indicated by the above threshold values to a maximum daily dose of 20 mg to achieve glucose control. If maximum daily dose of glyburide does not result in reaching the threshold values, patients will be administered insulin; however, data will be analyzed on an intent-to-treat basis. Continuous variables will be presented as mean +/- standard deviation, ordinal variables as medians, and dichotomous as percentages. Continuous data with normal distribution will be analyzed using unpaired (2sample) t-test. For more than 2 samples, analysis of variance (ANOVA, with possible repeated measures) will be used to analyze differences in outcome. Non-parametric equivalent tests will be used to compare ordinal variables or continuous variables not normally distributed. Categorical variables will be compared with the chi-square or Fisher exact test. Odds ratios will be calculated, with 95% confidence intervals. Logistic regression may be needed to adjust for confounding variables.

**Progress:** This protocol was closed to enrollment at MAMC due to difficulties with recruitment (many potential candidates were beyond the 34 week time of diagnosis) and low enrollment. Eight patients were enrolled; three were randomized to Glyburide and five to insulin. No patients on Glyburide had adverse reactions; however, two failed Glyburide treatment and were switched to insulin. This protocol will remain ongoing at MAMC until the protocol is completed at TAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206099	<b>Status:</b> Ongoing
<b>Title:</b> Molecular mechanisms of progesterone mediated inhibition of LPS and other inflammatory agent induced production of pro-inflammatory cytokines in the fetal-maternal circuitry of the human placenta		
<b>Principal Investigator:</b> MAJ Demetrice L. Hill, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Damian J. Paonessa, MC, USAF; MAJ Jennifer L. Gotkin, MC; CPT Jeremy P. Celver, MS; Heidi M. Cederholm, B.S.; James R. Wright, BA, MT (ASCP); LTC Peter G. Napolitano, MC		
<b>Start - Completion:</b> 6/16/2006 - Apr 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To identify the molecular mechanisms by which progesterone modulates pro inflammatory cytokine production following LPS and other inflammatory agent treatment of cells and tissue within the fetal/maternal circuit of the human placenta. Analysis will include ELISA, immunocytochemistry, western, antibody array, and high throughput proteomics.

**Technical Approach:** Placentas from normal women undergoing elective cesarean delivery prior to the onset of labor will be obtained within 15 minutes of delivery. At the time of cord clamping, 20cc of fetal cord blood will be obtained, spun down and the white blood cells collected and exposed to 50mg/ml lipopolysaccharide and evaluated using 1D or 2D gel electrophoresis. Additionally, both umbilical arteries will be gently and thoroughly flushed with Dulbecco's modified Eagle's medium (Gibco, Grand Island, NY) until the chorionic plate placental arteries are grossly free of blood. The arteries will be dissected from the placenta, carefully separating connective tissue from the endothelium. Eight contiguous segments of the umbilical artery (approximately 5 mm each) will be weighed and cultured in 6-well dishes (four per well) in either Hanks Balanced Salt Solution (HBSS) or Dulbecco's Modified Eagle's medium with Ham's F12 nutrient mixture (1:1) (DMEM/F12), antibiotics and 2 mmol/L glutamine in 5% carbon dioxide at 37C. Samples will be treated with 50ng/mL of lipopolysaccharide, lipopolysaccharide and medroxyprogesterone acetate (MPA) (50 ng/50 ng/ml), and MPA alone (50 ng/ml). Samples will be screened for total protein concentration by BCA analysis and specific induction of the inflammatory response by LPS will be verified with an Il6 or IL10 assay. Two placental explants from each group will be snap-frozen in liquid nitrogen and stored at -130C for possible total cellular proteomic analysis at a later date. The remaining placental explants will be stored in formalin at 4C and sectioned for immunohistochemical analyses as necessary.

Total protein from equal volumes of supernatant will be separated by 1D or 2D gel electrophoresis with the assistance of Dr Robert Allen, PhD. Separated proteins will be labeled in gel by coomassie blue and silver staining. MALDI-TOF (40.00/protein) will be used to identify proteins with dissimilar expression patterns (e.g., a consistent change between LPS and control in 2/3 of the tested samples). Immunohistochemistry, western analysis of 2D gels with commercially-available antibodies and ELISA analysis will validate the proteomic analyses when feasible. A SELDI-based proteomic analysis will also be considered depending on the effectiveness of the gel electrophoresis.

**Progress:** Ten samples have been evaluated. Large variations in the IL-6 production in response to LPS and LTA have been found. Factors are believed to be technician related. The protocol continues to collect samples and refine scientific techniques.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203067	<b>Status:</b> Ongoing
<b>Title:</b> The Effects of IL-10 on the Production of Inflammatory Cytokines in a Placental Artery Explant Model		
<b>Principal Investigator:</b> LTC Bobby C. Howard, MC, USAF		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrea D. Shields, MC; MAJ Christine M. Kovac, MC; LTC Peter G. Napolitano, MC		
<b>Start - Completion:</b> 4/30/2003 - Jun 2003	<b>Funding:</b> Air Force via MIPR	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** To determine the effects of IL-10 on placental artery production of inflammatory cytokines from normal patients.

**Technical Approach:** Maternal-fetal inflammatory states are associated with preterm labor, preterm premature rupture of membranes, preeclampsia, fetal growth restriction and fetal demise. It is also believed that cerebral palsy results from a fetal inflammatory response characterized by an environment of pro-inflammatory cytokines. IL-10 is a potent anti-inflammatory cytokine that has a potential role in the treatment of clinical septicemia by down-regulating the production of pro-inflammatory cytokines. Approximately 4 specimens will be studied here at MAMC.

**Progress:** This protocol has not yet initiated enrollment, pending preliminary data from another study that is currently in data analysis. Modifications may be required prior to initiating enrollment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203066	<b>Status:</b> Ongoing
<b>Title:</b> The Production of Immunoregulatory Cytokines in a Placental Artery Explant Model		
<b>Principal Investigator:</b> LTC Bobby C. Howard, MC, USAF		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrea D. Shields, MC; MAJ Christine M. Kovac, MC; LTC Peter G. Napolitano, MC		
<b>Start - Completion:</b> 4/30/2003 - Jun 2003	<b>Funding:</b> Air Force via MIPR	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** To determine the production of inflammatory cytokines from the placenta vessels of normal patients following endotoxin stimulation.

**Technical Approach:** Levels of two distinct cytokines, IL-6 and IL-10 will be determined. IL-6 is a Th-1 type cytokine that is implicated in cell-mediated damage in clinical states characterized by an inflammatory response. In contrast, IL-10 is responsible for down-regulating the TH-1 like response and has been demonstrated to inhibit the damage related to inflammatory states. By understanding the production rate of these cytokines by placental arteries at baseline and under stimulated conditions, it will enable us to study the potential therapeutic modalities to suppress the production of inflammatory cytokines. Approximately 4 specimens will be examined here at MAMC.

**Progress:** This protocol has completed specimen collection with a total of eleven patients consented in this study. Data analysis is currently ongoing.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204088	<b>Status:</b> Ongoing
<b>Title:</b> Use of Transvaginal Cervical Length Measurements in Twin Gestations		
<b>Principal Investigator:</b> LTC Bobby C. Howard, MC, USAF		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Peter G. Napolitano, MC; Samantha J. Thomas, RN		
<b>Start - Completion:</b> 9/17/2004 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** To determine if the use of routine transvaginal cervical length ultrasound can be used to prevent preterm deliveries in twin gestations.

**Technical Approach:** Twin gestations are one of the highest risk populations for preterm labor and ideal to use in this prospective randomized clinical trial to determine if the use of transvaginal cervical length measures can be used to improve perinatal outcome and prevent unneeded intervention in women destined to deliver at term. Subjects will be randomized to either routine management or serial transvaginal ultrasound assessments of cervical length. Subjects randomized to cervical length assessment will be managed according to a set protocol based on cervical length. Potential management options will include expectant management, activity restriction, frequent nursing contact, and/or offering cerclage placement. The primary outcome analysis will compare gestational age at delivery between groups.

**Progress:** This protocol closed to enrollment in May 2006, with seven patients enrolled at MAMC, one during FY06. Data analysis is ongoing.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 205005	<b>Status:</b> Ongoing
<b>Title:</b> The Distribution of Bishop Scores and Quantitative Values of Fetal Fibronectin (fFN) in Nulliparous Patients Between 37-42 Weeks Gestation: A Prospective Observational Study			
<b>Principal Investigator:</b> CPT Alison L. Lattu, MC			
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Bobby C. Howard, MC, USAF; LTC Peter G. Napolitano, MC; COL Peter E. Nielsen, MC; MAJ Shad H. Deering, MC; Kathleen T. Gardner, RN			
<b>Start - Completion:</b> 3/11/2005 - Feb 2006	<b>Funding:</b> Adeza Biomedical Corp via Geneva Foundation		<b>Periodic Review:</b> 9/29/2006

**Study Objective:** To evaluate the distribution of Bishop scores and quantitative values of fetal fibronectin (fFN) in nulliparous patients between the ages 18 - 40 and between 37 weeks through 42 weeks gestation. The secondary objective is to estimate the predictive value of Bishop scores and fetal fibronectin (fFN) testing in predicting delivery outcome (e.g. vaginal or cesarean delivery) in nulliparous patients between 37 weeks through 42 weeks gestation. The third objective is to compare the concordance and statistical agreement between matched fFN test results collected with a speculum and fFN tests results collected without a speculum. In this pilot study sample size is not necessarily sufficient for conclusive results.

**Technical Approach:** This is a prospective observational clinical study in women between the ages of 18 through 40. Between 37 weeks through 42 weeks gestation and following verification of inclusion criteria, fFN testing of cervicovaginal specimen obtained from the lower one-third of the vagina, fFN testing of a cervicovaginal specimen obtained with a speculum and digital cervical exam for the evaluation of Bishop score at the time of their routine prenatal visit. All patients meeting inclusion criteria and who consent to participation will have the following information recorded: patient's age, gestational age, dating criteria, presentation (and how this was assessed), fetal fibronectin test results, Bishop score (specifically, cervical dilation, effacement, station, position, and consistency), and whether or not membrane sweeping was performed. Information will be obtained regarding the most recent time of intercourse and cervical exam. Following delivery, the following information about the patient will be obtained: gestational age at time of admission for delivery, Bishop score (cervical dilation, station, effacement, position, and consistency) at time of admission, indication for admission, whether labor onset was spontaneous, induced, or augmented, length of hospital stay, time from admission to delivery, mode of delivery and birth weight. Additionally, data regarding the presence of the following maternal and fetal complications will be collected: fetal macrosomia (birth weight >4000gm), pre-eclampsia, chorioamnionitis, endomyometritis, meconium stained amniotic fluid, NICU admission, and intrauterine fetal death.

**Progress:** This protocol remains open to enrollment with 135 patients enrolled to date; 115 patients received diagnostic testing, fourteen were not tested/lost to follow up, three delivered before testing began, and three withdrew consent. Investigators are currently analyzing interim data but plan to continue the protocol until full enrollment has been reached. Plan to present some of the interval data at the annual American College of OB/Gyn Clinical Meeting in May.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203078	<b>Status:</b> Ongoing
<b>Title:</b> Use of Pipelle Endometrial Sampling in the Evaluation of Abnormal First Trimester Pregnancy		
<b>Principal Investigator:</b> CPT Alison L. Lattu, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Gregory E. Chow, MD; LTC Michael K. Chinn, MC; CPT Harlan I. Rumjahn, MC; CPT Joren B. Keylock, MC		
<b>Start - Completion:</b> 8/27/2003 - Sep 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/10/2006

**Study Objective:** To evaluate the sensitivity of endometrial sampling in the detection of intrauterine products of conception in abnormal gestations.

**Technical Approach:** This study will look at patients undergoing evaluation and management for abnormal gestations who have opted for surgical management with dilation and curettage (D&C). This will not include patients undergoing emergency procedures. Approximately 100 patients will be enrolled into this study here at MAMC. The patient will have a pipelle endometrial sampling performed prior to the D&C. This procedure consists of a pipelle being inserted in to the uterine fundus and drawing it back and forth for 15-30 seconds to obtain a sample of the endometrial tissue and uterine contents. This sample will be transferred to a 10% formalin solution and then taken to the pathology department at MAMC for processing and evaluation.

**Progress:** Interim data analysis has been completed with sensitivity of EMBX 73% and 92% for curettage. No adverse outcomes. Investigators will consider whether or not to proceed with continued enrollment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205089	<b>Status:</b> Ongoing
<b>Title:</b> Pilot Study of a Novel Cord Blood Collection Technique		
<b>Principal Investigator:</b> CPT Megan M. Manshande, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC; LTC Peter G. Napolitano, MC; COL Jerome B. Myers, MC; CPT Mitchel T. Holm, MC; CPT Jeremy P. Celver, MS; Carol D. Dean, RN, BSN		
<b>Start - Completion:</b> 5/26/2005 - Apr 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** Primary Objective: To demonstrate the feasibility of a novel technique for umbilical cord blood collection after delivery. Secondary Objective: To compare this method of collection to historical results obtained from medical literature.

**Technical Approach:** After collecting umbilical cord blood via the method proposed in this protocol, investigators will compare blood volumes and the number of hematopoietic progenitor cells harvested to historical controls. Investigators propose that this new method of cord blood collection after delivery will allow collection of a larger volume of umbilical cord blood than the currently used standard method of cord blood collection thus allowing harvest of a larger number of stem cells. Development of a collection technique which would give a higher yield of stem cells would broaden the range of transplant options available for adult recipients.

**Progress:** Investigators have now obtained the proper equipment kits to collect samples and will have all samples collected within the next two months. Two patients were enrolled in the study since its approval, but will not be included in the final data because investigators were perfecting the collection technique prior to actually collecting samples to include in the study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203045	<b>Status:</b> Ongoing
<b>Title:</b> Randomized Controlled Trial of Endurance Exercise and Gallbladder Disease Risk in Overweight Pregnant Women		
<b>Principal Investigator:</b> LTC Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Sum P. Lee, M.D., Ph.D; Shirley Beresford, Ph.D; Cynthia Ko, M.D.; Anne McTiernan, M.D.; Deborah J. Bowen, Ph.D; LTC James K. Howden, MC; COL Peter E. Nielsen, MC; Scott J. Schulte, M.D.; Mary Emond, Ph.D		
<b>Start - Completion:</b> 1/27/2004 - Jan 2008	<b>Funding:</b> UW via The Geneva Foundation	<b>Periodic Review:</b> 1/24/2006
<b>Study Objective:</b> (1) To evaluate whether an endurance exercise program is associated with lower risk of gallbladder disease in overweight pregnant women. (2) To evaluate whether an endurance exercise intervention program changes leptin levels in pregnancy among overweight women. (3) To use statistical methods to examine the associations between gallbladder disease incidence and potential causal variables in this prospective trial. These variables include baseline levels of leptin, HDL, insulin levels, BMI (as it varies within women classified as overweight) and changes in these variables. Secondly, we aim to estimate the degree of compliance and overall adherence to an exercise intervention in normal weight pregnant women, in the context of a randomized intervention study.		
<b>Technical Approach:</b> This trial will evaluate the effect of an intervention designed to increase regular endurance exercise of moderate to vigorous intensity on the risk of gallbladder disease in pregnancy.. Women will be stratified according to overweight or normal weight status. The randomized controlled trial will be confined to the former group (n=862), while a feasibility trial will be conducted among 250 normal weight women. The comparison groups will receive the exercise intervention in the post-partum period. They will continue their usual activities during pregnancy. Thus all women participating in the trial will receive the benefit of exercise training at some point during the study period. The study population will be pregnant women aged 18 to 45. All women presenting for prenatal care will be potentially eligible. Additional clinical procedures specific to the study include a first and third trimester ultrasound of both the gallbladder and the fetus, and an additional blood draw at those times. Usual care includes a second trimester ultrasound of the fetus, to which will be added an ultrasound of the gallbladder, and a blood draw, to which additional tubes will be added. To enhance cooperation with additional study procedures in the exercise intervention study, we will provide a \$30 financial incentive for completing the 1st trimester and late 3rd trimester blood draws. This incentive will not be provided for the early 3rd trimester blood draw, since it occurs at the same time as a routine prenatal blood draw. As an added incentive to participate, an additional scan of the fetus will be made at the first trimester gallbladder ultrasound examination. This will allow women an early glimpse of their baby. For women who have other children, we will provide a reimbursement for childcare expenses (\$3 per hour) during exercise or stretching classes. Pedometers will be provided during the study for the intervention group, and at the postpartum visit for the control women.		
<b>Progress:</b> This protocol remains open to enrollment, with 3,707 women contacted, 846 women who agreed to enroll and 443 who completed the study. Of this group, 204 were disqualified because of gallstones, miscarriage or failure to comply with study requirements/medical conditions. Expanding the BMI range to 34.9 has allowed enrollment of 38 additional women that would not of qualified.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203001	<b>Status:</b> Ongoing
<b>Title:</b> The Effect of Magnesium on Matrix Metalloproteinase-9 Activity in Umbilical Cord Blood at Delivery of Pregnancies Complicated by Chorioamnionitis		
<b>Principal Investigator:</b> LTC Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Patrick M. McNutt, MS; Lisa M. Pierce, D.Sc.; MAJ Christine M. Kovac, MC; LTC Bobby C. Howard, MC, USAF; MAJ Brian T. Pierce, MC; LTC Nathan J. Hoeldtke, MC		
<b>Start - Completion:</b> 7/29/0030 - Dec 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To determine baseline umbilical cord serum levels of matrix metalloproteinase-9 levels at delivery in pregnancies where labor is complicated by chorioamnionitis compared to normal term controls. To determine if magnesium will reduce the enzymatic activity of serum matrix metalloproteinase-9 in the umbilical cord plasma of neonates from pregnancies complicated by chorioamnionitis compared to normal controls.

**Technical Approach:** Matrix metalloproteinases are zinc-dependent enzymes and it is possible that ionized magnesium which easily crosses the placenta could competitively inhibit MMP-9 enzyme by displacing zinc. We propose to test this hypothesis by first determining what normal levels of MMP-9 enzyme are in pregnancies complicated by infection (those complicated by chorioamnionitis in labor) compared to normal pregnancies with normal labors. Since it would not ethically be acceptable to administer Magnesium sulfate a tocolytic to such complicated pregnancies, we will collect the plasma of such pregnancies then expose it ex vivo to similar levels of magnesium that would be expected if we had treated the mother with standard therapy. Then assay those samples for MMP-9 enzyme activity.

**Progress:** Bench top research completed, paper submitted but rejected, and awaiting changes to be made and resubmission. This study remains open as investigators may need to collect more specimens, based on peer review of findings.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203099	<b>Status:</b> Ongoing
<b>Title:</b> Umbilical Cord Plasma Homocysteine Concentrations at Delivery in Pregnancies Complicated by Preeclampsia		
<b>Principal Investigator:</b> LTC Peter G. Napolitano, MC		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Christopher S. Murphy, MC; CPT Charles L. Wakefield, MC		
<b>Start - Completion:</b> 8/1/2003 - Dec 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/20/2006

**Study Objective:** The purpose of this study is to evaluate the level of umbilical cord plasma homocysteine in gestations complicated by pre-eclampsia compared to normotensive gestations.

**Technical Approach:** General Protocol Sampling Umbilical cord blood samples will be obtained immediately after cord clamping by direct venipuncture of the umbilical vein collected in lavender top tubes. The specimens will be stored on ice and centrifuged at 3000 rpm for 15 min as soon as possible. After extracting the serum plasma, it will be divided into several aliquots for storage. All specimens will be frozen and maintained at -70o C. Maternal plasma obtained at the time of routine labor admission blood work will be collected and stored in a similar fashion. At four points during the study, the specimens will be collected and sent to William Beaumont Army Medical Center, TX, Dept of Pathology for homocysteine level analysis. A sample of 1mL of EDTA plasma is necessary for laboratory analysis. The plasma homocysteine level is measured by ADVIA Centaur HCY assay. Each specimen will be run in duplicate.

**Progress:** This protocol remains open to enrollment. No new patients were enrolled since the last progress report. The protocol was amended to allow inclusion of patients with Preterm preeclampsia and Preterm preeclampsia with IUGR, although recruitment of patients did not occur. Recruitment and enrollment is expected to begin with the addition of a new associate investigator, Dr Christopher Murphy. At this time, data analysis has been performed on ten control patients and eight patients with pre-eclampsia. There was a significant difference between HCY levels in the pregnancies complicated by pre-eclampsia and the control patients (maternal and fetal).

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204108	<b>Status:</b> Completed
<b>Title:</b> The Effects of Cholic Acid and Deoxycholic Acid on Placental Artery Perfusion Pressures in the Ex Vivo Placental Cotyledon Model		
<b>Principal Investigator:</b> LTC Damian J. Paonessa, MC, USAF		
<b>Department:</b> OB/GYN	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Nathan J. Hoeldtke, MC; LTC Peter G. Napolitano, MC; LTC Bobby C. Howard, MC, USAF; MAJ Andrea D. Shields, MC; MAJ Jennifer L. Gotkin, MC		
<b>Start - Completion:</b> 8/31/2004 - May 2005	<b>Funding:</b> Air Force via MIPR	<b>Periodic Review:</b> 8/22/2005

**Study Objective:** To determine if infused concentrations of cholic acid and deoxycholic acid affect placental artery perfusion pressures.

**Technical Approach:** This bench study will evaluate the placental vascular tone after exposure to the bile salts cholic acid and deoxycholic acid. Placentas from normal women will be obtained within 15 minutes of delivery. Fetal surface will be inspected for a chorionic artery and vein pair supplying a functional cotyledon. Although wavier of informed consent was appropriate, investigators chose to utilize a consent form to obtain permission for use placentas under this bench research protocol.

**Progress:** The PI reported this protocol completed in June 2006; he is in the process of data analysis. Nine placentas were collected; three did not survive the attempt to collect data.

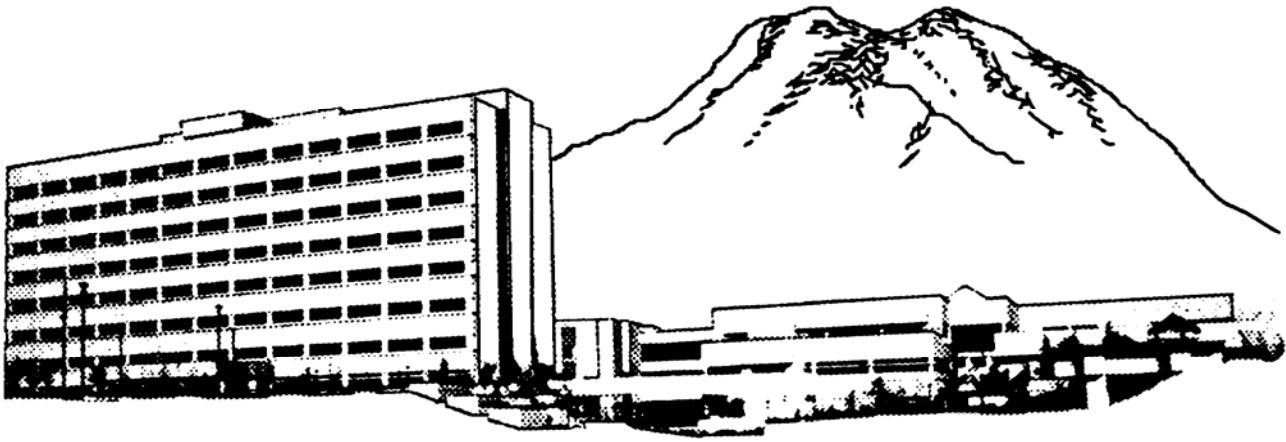
## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205021	<b>Status:</b> Ongoing
<b>Title:</b> Correlation of Persistent Anal Sphincter Defects and Symptoms following Repair of Anal Sphincter Lacerations due to Obstetric Injury in Primiparous Women		
<b>Principal Investigator:</b> CPT Christine M. Zalucki, MC		
<b>Department:</b> OB/GYN		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Jeffery L. Clemons, MC; CPT Rhiana D. Saunders, MC		
<b>Start - Completion:</b> 12/10/2004 - Jan 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11/21/2006

**Study Objective:** To identify the incidence of persistent anal sphincter defects following repair of anal sphincter lacerations (ASL) due to obstetric injury in primiparous women. To correlate the size of the persistent anal sphincter defect (ASD) with anal incontinence symptoms. To identify the size of ASD at which symptoms increase dramatically, if any. To identify risk factors for symptomatic ASD.

**Technical Approach:** A prospective observational study will be conducted over a 24 month period. Primiparous women that have sustained an ASL and undergone successful repair will be recruited during their postpartum stay at MAMC. Obstetric records will be reviewed to collect demographic data, medical history, delivery outcomes, and anal sphincter repair technique. At 8 weeks postpartum, each woman will undergo endoanal sonography and complete the Wexner anal incontinence questionnaire. The endoanal ultrasound will be used to detect and measure the size of ASD. A persistent ASD will be defined as any defect of the integrity of the IAS or EAS. Photographic images will be taken of the largest portion of the ASD. The size of the defect (in degrees) will be measured by a protractor. The length of the defect (in millimeters) will be measured by 3-D ultrasound. Three researchers will perform all measurements. The endosonographer will be blinded to the questionnaire results. The Wexner anal incontinence questionnaire assesses the presence and frequency of incontinence to flatus, liquid and solid stool, pad use, and lifestyle alteration. Scores can range from 0 (complete continence) to 20 (severe incontinence to solid stool on a daily basis). A score of 4 or more at 2 months post-partum will define a symptomatic ASD. Women with and without symptomatic ASD will be compared to identify risk factors for symptomatic ASD. Approximately 72 women with ASD will be needed to demonstrate a difference in defect size between symptomatic and asymptomatic ASD. Demographic and delivery data will be entered onto a Data Sheet. The ultrasound data and questionnaire data will be also entered onto the Data Sheet. All data will then be transferred to the Excel spreadsheet. Security issues will be enforced (locking computer and office).

**Progress:** This protocol completed the enrollment phase with a total of 47 patients enrolled at MAMC over the 20 month enrollment period. Patients will continue to be followed by phone through FY07. The study found that an injury to the internal anal sphincter  $\geq 45$  degrees was strongly associated with anal incontinence symptoms. Also, the anal sphincter laceration rate at MAMC is 3%, and persistent defect rate is 79%. No risk factors were identified for persistent anal sphincter defects. One patient underwent overlapping sphincteroplasty for severe anal incontinence.



# Detail Summary Sheets

Department of Pathology



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203095	<b>Status:</b> Terminated
<b>Title:</b> Implementation of the SARS Coronavirus Real-Time PCR Primers and Probes Assay to Detect SARS Coronavirus in Respiratory Specimens		
<b>Principal Investigator:</b> MAJ Edward P. Ager, MS		
<b>Department:</b> Pathology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Steven D. Mahlen, MS; COL Joseph T. Morris III, MC; LTC David K. Turgeon, MC; LTC James E. Cook, MC; CPT Sheryl A. Bedno, MC		
<b>Start - Completion:</b> 5/12/2004 - Jul 2004	<b>Funding:</b> CDC via MIPR	<b>Periodic Review:</b> 7/1/2005

**Study Objective:** To use real-time PCR assays to detect SARS Coronavirus RNA in respiratory specimens and as a surveillance tool allowing public health laboratories to respond to the outbreak and limit transmission of this agent.

**Technical Approach:** This protocol describes a plan to export the current CDC SARS Coronavirus real-time PCR assay to participating public health laboratories and clinical diagnostic laboratories within the Laboratory Response Network (LRN) for use in diagnostic evaluation of SARS Coronavirus infection. Fifty patients will be enrolled for this protocol, and two sets of specimens will be taken from each subject. One set of specimens will be shipped to the CDC for testing; the other set of specimens will be tested for the SARS Coronavirus at MAMC. SARS Coronavirus detection data will be collected for this study, and compared with results obtained from the CDC.

**Progress:** A change PI was approved from MAJ Steven Mahlen, MS, to MAJ Edward Ager, MS, Staff Department of Pathology. The protocol was terminated 15 May 2006, with no subjects enrolled. No human infection with the SARS coronavirus was identified in over 2 years.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203041	<b>Status:</b> Ongoing
<b>Title:</b> Use of a Non-FDA Approved Gene Amplification Test To Detect or Rule-Out Vaccinia in Patients With Complications Following Smallpox Vaccination or Possible Contact Vaccinia		
<b>Principal Investigator:</b> MAJ Edward P. Ager, MS		
<b>Department:</b> Pathology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Steven D. Mahlen, MS; COL Joseph T. Morris III, MC; COL Mary P. Fairchok, MC; LTC Peter G. Napolitano, MC		
<b>Start - Completion:</b> 4/30/2003 - Mar 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7/20/2006

**Study Objective:** To determine the sensitivity, specificity and clinical utility of the only test currently available to detect vaccinia virus in patients who may be experiencing post-vaccination complications following smallpox vaccination, or in close contacts of vaccinees who may have been inadvertently inoculated with the vaccinia virus (contact vaccinia).

**Technical Approach:** Clinicians seeing patients with possible post-vaccination complications or suspected contact vaccinia will collect and submit three swabs of lesion fluid to one of the DOD Confirmatory Labs with the vaccinia test. One swab will be used for vaccinia PCR using either the Cepheid SmartCycler or the Idaho Technology LightCycler platforms that are approved as LRN tools. DNA extraction and amplification will be done strictly following the LRN protocol. Extraction of DNA from exudate material and specimen processing will take approximately 2 hours. Amplification results will be final approximately 30 minutes after the amplification begins. A positive amplification result is determined by standardized parameters and with a calculated threshold done by the real-time PCR unit. The second swab will be used for viral culture. Vaccinia virus produces cytopathic effects (CPE) in most common cell lines used in clinical virology labs. The CPE resemble those of HSV, CMV and adenovirus. While clinical labs can rapidly identify HSV, adenovirus and CMV in infected cell lines using DFA, there is no such test for vaccinia. However, if a specimen results in CPE, but is negative for HSV, adenovirus and CMV by DFA, then that culture may be a presumptive result for vaccinia, and will be result as "CPE from lesion material - negative for HSV, adenovirus, and CMV". Specimens with no resultant CPE will be finalized as "No virus detected". The third swab will be submitted for bacterial culture and sensitivity (standard of care). Viral and bacterial culture data, along with PCR data will be used in conjunction with the clinical situation to help determine if the patient has post-vaccinial complications due to vaccinia virus, contact vaccinia, or is experiencing rashes or lesions due to other causes. All specimens kept at the DOD LRN Confirmatory Labs will be handled and disposed of in accordance with federal regulations.

**Progress:** This protocol remains open to patient entry, with six patients enrolled, one during FY06. This is a CDC Protocol and as such is conducted under auspice of the CDC IRB.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205102	<b>Status:</b> Ongoing
<b>Title:</b> Absolute Lymphocytosis in Adults: A Laboratory Protocol		
<b>Principal Investigator:</b> CPT Jared M. Andrews, MC		
<b>Department:</b> Pathology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Mitchel T. Holm, MC; COL Jerome B. Myers, MC		
<b>Start - Completion:</b> 7/12/2005 - Oct 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/12/2006

**Study Objective:** The objective is to analyze and report correlations between diagnosis rendered by flow cytometry analysis of patients with peripheral blood lymphocytosis, and the lymphocyte counts and other demographics of the patients. International guidelines for flow cytometric analysis of peripheral blood lymphocytosis to rule out leukemia/ lymphoma are not well defined. These correlations can be used to help develop hospital protocols for the evaluation of absolute lymphocytosis in adults.

**Technical Approach:** This is a retrospective, descriptive study of Madigan Army Medical Center's process for analysis of peripheral blood lymphocytosis in persons greater than 18 years of age. By analyzing the demographic data, CBC, and flow cytometrical results obtained, it is our hypothesis that this information can be beneficial in more accurately defining guidelines for the use of flow cytometry for lymphocytosis, and promote further prospective research in this area.

**Progress:** This protocol has completed data collection and statistical analysis and remains ongoing to complete final manuscript of findings.

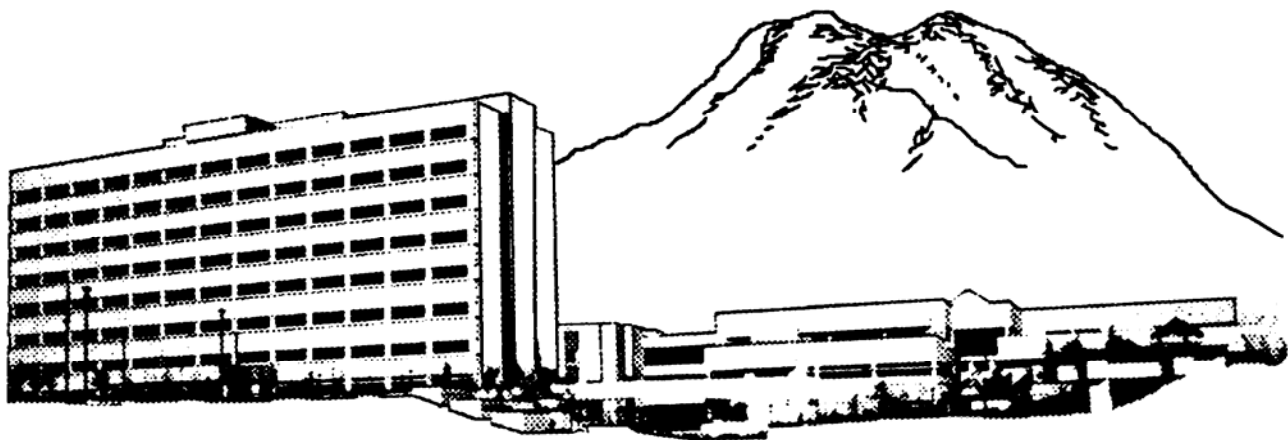
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205042	<b>Status:</b> Ongoing
<b>Title:</b> Incidental Anatomic and Histologic Findings in Bariatric Surgery Specimens		
<b>Principal Investigator:</b> MAJ Anne L. Champeaux, MC		
<b>Department:</b> Pathology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ James B. Branch, MC; CPT Vance Y. Sohn, MC		
<b>Start - Completion:</b> 2/14/2005 - Apr 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/26/2006

**Study Objective:** Collection, review and compilation of anatomic/histologic findings in bariatric surgery specimens processed by Madigan Army Medical Center (MAMC) Department of Pathology, Anatomic Pathology Service from 1994-2004.

**Technical Approach:** Collection, review and analysis of bariatric surgery specimen reports generated by the MAMC Anatomic Pathology service from 1994 through 2004 to identify and correlate anatomic and histologic findings with age and gender. The study aims to elucidate the range of anatomic and histologic variables found in partial gastrectomy, gallbladder and appendices removed during bariatric procedures.

**Progress:** This protocol was suspended in February 2006, pending completion of the continuing review process. PI intends to request IRB approval to increase the number of patient cases and records up to 600 and add an associate investigator.



# **Detail Summary Sheets**

## **Department of Pediatrics**

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203014	<b>Status:</b> Terminated
<b>Title:</b> Clinical Use of Reticulocyte Hemoglobin to Detect Iron Deficiency at the 12 Month Well Baby Visit		
<b>Principal Investigator:</b> CPT Rochelle L. Cason, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Athena J. Stoyas, MC; LTC Robert G. Irwin, MC; COL Kelly J. Faucette, MC; Elizabeth N. Hasert, MD		
<b>Start - Completion:</b> 3/4/2003 - May 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/28/2004

**Study Objective:** To determine if the reticulocyte hemoglobin is a more sensitive and specific marker than hemoglobin and hematocrit for iron deficiency at the 12 month well child visit.

**Technical Approach:** This is a prospective study that will evaluate the utility of reticulocyte hemoglobin as a screen for iron deficiency and iron deficiency anemia in comparison to current measures of hemoglobin and hematocrit. All infants that present for their 12 month well child check and any infants 9 to 18 months with a clinical indication or who have missed their 12 month well baby visit will have screening hemoglobin, hematocrit, and reticulocyte hemoglobin. If either hemoglobin, hematocrit, or reticulocyte hemoglobin are low these patient's will be placed on iron therapy. The three treatment groups will include: 1. Decreased hemoglobin, hematocrit, and reticulocyte hemoglobin; 2. Decreased hemoglobin and/or hematocrit. Normal reticulocyte hemoglobin; 3. Normal hemoglobin and hematocrit. Decreased reticulocyte hemoglobin. After one month of therapy a repeat venous hemoglobin, hematocrit, and reticulocyte hemoglobin will be checked. If these measurements show improvement as previously defined, the patient will be diagnosed with iron deficiency and/or iron deficiency anemia and will continue on two more months of iron therapy. Measurements of hemoglobin and hematocrit and reticulocyte hemoglobin will be compared in their sensitivity and specificity in detecting iron deficiency and iron deficiency anemia. If group 1 shows improvement in all tested variables, this would suggest that reticulocyte hemoglobin correlates well with hemoglobin and hematocrit measurements. If group 3 responds to therapy and group 2 does not respond to therapy this would indicate that reticulocyte hemoglobin is a more sensitive and specific indicator of iron deficiency. 60 patients will be placed into each group. Once 30 patients are in each group an interim analysis, using chi square, of the data will be obtained to assess if there is statistical significance.

**Progress:** The IRB terminated this protocol in August 2006, when no principal investigator was assigned by the Department of Pediatrics during the study's last approval period. The protocol had been suspended at the request of associate investigator, Dr. Hasert, until a new PI could be assigned. The last report noted 57 of 500 patients enrolled with 7 positive results that support the study hypothesis.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 204104	<b>Status:</b> Ongoing
<b>Title:</b> Health, Quality of Life & Activity in Cerebral Palsy			
<b>Principal Investigator:</b> COL Beth E. Davis, MC			
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Robert L. Miller, MC; Kristie Bjornson, PhC, PT			
<b>Start - Completion:</b> 9/13/2004 - Jun 2006	<b>Funding:</b> United Cerebral Palsy Research & Education Foundation via Grant		<b>Periodic Review:</b> 8/10/2006

**Study Objective:** Aim 1. To test for differences in activity performance, self and parent reported health status and QOL (Quality Of Life) among youth with CP (Cerebral Palsy) and TDY (Typically Developing Youth) by level of activity capacity, while controlling for baseline activity performance and capacity, age, gender, SES and current day outlook. The predicted differences in activity performance, self-reported health status will be such that TDY will be greater than CP youth (TDY > CP), and that these differences will be ordered by defined levels of activity capacity with the Gross Motor Function Classification System (GMFCS) such that TDY > Level I > Level II > Level III, while controlling for baseline activity performance, age, gender, SES and current day outlook. The predicted differences in QOL will not be ordered by activity capacity.

Aim 2. To examine the associations between activity level (performance) and self and parent perceived health status and QOL in youth with CP and TDY, while controlling for baseline activity performance and capacity, age, gender, SES and current day outlook. There will be a positive linear relationship by activity capacity level (GMFCS) between activity performance and the health status physical domain (Child Health Questionnaire, CHQ-P). There will be a positive linear relationship by activity capacity (GMFCS) between activity performance and the QOL relationship domain (Youth Quality of Life, YQOL-R). The relationship of activity performance to the health status psychosocial domain (CHQ-PS) and the QOL self, environment and general QOL (YQOL-R: S, E & GQOL) will not be linear by activity capacity level.

Aim 3. Explore a model specifying the influence of activity capacity and activity performance on health status and quality of life controlling for baseline activity performance, age, gender, SES, and current day outlook.

**Technical Approach:** This is a multi-center study that intends to study the health, quality of life, and activity in children with cerebral palsy. Children with the diagnosis of cerebral palsy, Gross Motor Function Classification System (GMFCS) levels I-III and typically developing youth, ages 10 to < 14 years, with the ability to read and understand at the 10 year age level will be studied. 30 children with cerebral palsy and 10 children that are typically developing that meet inclusion criteria through the MAMC study site will be enrolled, as well as one parent/guardian of each child enrolled (40 parents). Potential study participants will be recruited through a focused direct mailing of an approach letter introducing the project to the guardians of children with CP and typically developing youth that have had medical care at the MAMC Developmental Pediatrics, General Pediatrics, and Family Practice clinics. An informational letter will be sent to school based nurses, physical and occupational therapists, or other health care providers at military facilities in Western Washington. The letter will introduce the project, state that ambulatory children with CP and TDY are being sought for participation in the study, the inclusion criteria and brief description of the project. Local health care providers can then approach their patients about interest in the study and give them the contact information of the PI and/or contact the PI for further information about the project.

Once consent and assent have been attained, there will be two research visits seven days apart in the participants' home at their convenience. At the first visit, the youth will be asked to complete the questionnaires and have the Step Watch calibrated to their walking pattern. They will be asked to wear the Step Watch for seven days. On day seven, researchers will return to their home to download the information from the Step Watch and complete appropriate questionnaires. Parents/ guardians will be asked to complete the appropriate questionnaires on visit day one and visit day seven. For specific primary and secondary outcomes, design and procedures, data preparation, and analysis, see sections 9.3 through 9.6 in the Master Protocol.

**Progress:** Data collection was completed for twenty MAMC subjects, sixteen during FY06. Data collection continued for subjects in specific categories of impairment related to their CP from the CHRMC research office, for a total of over 100 patients with cerebral palsy. This was completed in December 2005. Data analysis began and Principal PI at CHRMC (K. Bjornson) defended PhD dissertation with results. The protocol remains ongoing at MAMC. Initial manuscript preparation underway regarding the scope of activity recorded for varying degrees of physical impairment in children with cerebral palsy.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204074	<b>Status:</b> Ongoing
<b>Title:</b> Survey of Chronic Pain and Its Effects on Youth With Disabilities		
<b>Principal Investigator:</b> COL Beth E. Davis, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Joyce M. Engel, PhD, OTR/L; Kenneth M. Jaffe, M.D.; John F. McLaughlin; Mark P. Jensen, PhD; Dawn Ehde, PhD		
<b>Start - Completion:</b> 6/16/2004 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/10/2006

**Study Objective:** This study has two specific aims: (1) to increase our understanding of the frequency and severity of pain problems in youth with spina bifida (SB), muscular dystrophy (MD), cerebral palsy (CP), limb deficiency (LD), and spinal cord injury (SCI); and (2) to develop a biopsychosocial model for the study of chronic pain in youth with disabilities.

**Technical Approach:** This study uses a cross sectional design. A convenience sample of 100-150 youths will be interviewed in-person or over the telephone to complete a standardized questionnaire on pain. The youths' parent/guardian will also be invited to complete a questionnaire (assistance will be provided as needed). Subject inclusion criteria include: a primary diagnosis of CP, LD, SCI, SB, or MD, a chronological age range of 8-to-20 years, capacity for expressive communication which may include the use of augmentative communication devices, English as the primary language, and no more than mild cognitive impairment. Subjects will be paid \$40.00 (\$25.00 for youth and \$15.00 for parent/guardian) for the completion of interview/questionnaire. Potential subjects will first be contacted directly by Dr. Beth Ellen Davis or medical personnel involved in the care of the youths, via an approach letter mailed by Dr. Davis, or posting of a recruitment flyer. Parents/guardians and young adults who are interested in the study will be asked to return an interest/information form in the provided postage-paid envelope to Dr. Davis at the Developmental Pediatrics Clinic at Madigan Army Medical Center. Dr. Davis will then inform UW investigators via confidential e-mail, a letter sent through the mail or telephone calls of those families interested in participating. UW research personnel will then contact these potential subjects. Interested parents/guardians or youth may also contact the principal investigator or study project director via e-mail or telephone. At the time of the contact, the purpose and procedures of the study will be explained and the parent/guardian will have the opportunity to ask questions. If the parent/guardian and youth express interest in the participating in the study, the investigator will screen to insure that all inclusion criteria have been met including a brief cognitive screening. If the inclusion criteria are met, an interview will be scheduled at a time and place (University of Washington Medical Center, the subject's home, or over the telephone for youths without speech difficulties) that is most convenient for the subjects. Assent and consent forms will be completed by the youth and parent/guardian prior to the initiation of the interview/questionnaire. A brief, standardized cognitive screening will also be completed prior to initiation of the interview (youth subject must score a minimum of 17/25 on the modified Mini Mental Status Examination to be eligible for participation. A subject descriptive information sheet will be completed. The youth will then be interviewed in-person or over the telephone by a study investigator or trained research assistant while the parent/guardian completes a disability specific form and a written questionnaire. The youth's interview and parent/guardian questionnaire each will take approximately 10 to 50 minutes to complete depending on whether or not the youth reports recurrent, bothersome pain. Response keys are used throughout the interviews to facilitate answering questions. All data will be entered into MS ACCESS. After all data have been entered, variables will be inspected for outliers and skewness and adjusted using appropriate transformations. Descriptive analysis will then be performed.

**Progress:** In the last year, 36 dyads (parent and youth with spina bifida) have completed various (11) comprehensive surveys regarding pain and its effects on daily living. An abstract describing the early results of the nature and scope of pain in youth with spina bifida was accepted for presentation at two national meetings: Poster presentation at AACPDM, Orlando Fla. 15 Sep 2005; research competition at the AAP Uniformed Services Pediatric Seminar, Portsmouth VA, March 13, 2006 where it came in Second Place in the military peer reviewed Margilith Research Award. Overall, descriptive information revealed that recurrent bothersome pain is common in youths with SB. Despite effectiveness of non-medical interventions, most participants reported use of opiates/narcotics as most helpful for their chronic pain symptoms. Manuscript preparation is underway. The protocol remains ongoing; the next step is to analyze the Quality of Life data with the reported pain frequency, intensity and locations.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206049	<b>Status:</b> Ongoing
<b>Title:</b> An Observational Study to Determine the Factors Influencing Bone Mineral Density in Post-Menarchal Adolescents with Neuromuscular Disabilities		
<b>Principal Investigator:</b> MAJ Michelle K. Ervin, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Beth E. Davis, MC; LTC Stephen M. Yoest, MC; COL (Ret) Patrick C. Kelly, D.O.; LTC Antonio G. Balingit, MC		
<b>Start - Completion:</b> 3/7/2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine bone mineral density measurements by use of DEXA technique at the distal femur, in a heterogeneous group of post-menarchal females with neuromuscular disabilities and compare to previously published reference data of age-matched normal controls. To describe the associations between bone mineral density measurement and multivariate factors such as: 1) anti-epileptic medication use, (2) mobility status as defined by the Gross Motor Function Classification System (GMFCS; see appendix for description of this scale), (3) Body mass index (BMI), (4) Tanner staging, and (5) hormonal contraceptive use while controlling for nutritional intake, specifically calcium and vitamin D.

**Technical Approach:** This observational pilot study will evaluate the bone mineral density in a heterogeneous group of 45 post-menarchal females ages 11 through 24 with neuromuscular disabilities that meet the inclusion criteria. The change in bone mineral density will be descriptively compared. Potential subjects will be recruited through a focused direct mailing of an approach letter introducing the project to the subject and/or guardians of eligible adolescent females receiving care at the Madigan Army Medical Center Pediatric Clinic, Adolescent Clinic, and Developmental-Behavioral Clinic. The letter will introduce the project, and state that post-menarchal females with neuromuscular disabilities are being sought for participation in the study, the inclusion criteria and a brief description of the project. Once consent, assent or surrogate consent has been obtained, a clinic appointment will be scheduled with a member of the investigative team to conduct an intake history and physical exam, and initiate dietary assessment through the use of a three day diet diary. Those participants identified as having insufficient calcium and/or vitamin D intake will be provided with supplemental therapy. Subjects will have distal femur bone mineral density measured at baseline, 6 months and 12 months. No current reference normative data exists for this population. Once all of the data is collected BMD measurements will be descriptively compared using multivariate logistical regression to determine significance of osteopenia risk factors identified for each subject.

**Progress:** This protocol remains open to enrollment, with 18 subjects enrolled during FY06. All 18 subjects completed the initial baseline bone mineral density scan, and one patient has returned for the six-month interval scan. The study staff is currently in the process of scheduling six-month interval scans for the remaining 17 subjects. The IRB recently approved an amendment to include a lumbar spine DEXA, along with the already approved distal femur DEXA when subjects return for their six-month and twelve-month follow up visits. One study patient died; however, this death was considered unrelated to study participation. Patient follow-up visits and study recruitment will continue during FY07.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205138	<b>Status:</b> Ongoing
<b>Title:</b> Evaluation of Serologic Responses to Fluzone® in Infants > 6 Months of Age Who Did or Did Not Receive Fluzone Vaccine at 2 Months of Age		
<b>Principal Investigator:</b> COL Mary P. Fairchok, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Sue E. Chambers, RN		
<b>Start - Completion:</b> 11/17/2005 - Sep 2006	<b>Funding:</b> Sanofi Pasteur via The Geneva Foundation	<b>Periodic Review:</b> 9/26/2006

**Study Objective:** To demonstrate the safety and immunogenicity of Fluzone vaccine administered in 6 month olds who have previously received this immunization compared to 6 month olds who have not received this vaccine previously.

**Technical Approach:** This is an observational and descriptive study that will provide preliminary comparative information about the safety and immunogenicity of Fluzone vaccine among children who were given Fluzone vaccine at 2 months of age as part of MAMC protocol 205034 (Group 1) versus children who have never received influenza vaccine (Group 2). All participants will be enrolled after obtaining informed consent from their parent or guardian.

At study visit 1, all participants will undergo informed consent, and a medical history and directed physical exam will be conducted. All participants will then receive one 0.25 mL intramuscular injection of Fluzone®. Both groups will be provided with a diary card to take home at this visit, recording solicited and unsolicited local and systemic adverse effects of the vaccines as well as daily temperatures for the 7 days after the visit.

At study visit 2, a blood sample will be collected from all subjects, and both groups will receive a second 0.25ml intramuscular injection of Fluzone®. Interim histories and diary cards will be collected and a second diary card will be provided.

At study visit 3, a blood sample will be collected from all subjects. Diary cards and interim history will be obtained. There will be a follow up contact by phone of all study participants at 6 months after visit the last dose of Fluzone® to solicit adverse events.

Other, non-study, vaccinations may be given at any study visit or at any time beginning 15 days following Visit 2. No vaccinations may be given between Visit 1 and Visit 2, nor in the 14 days preceding Visit 1 or following Visit 2.

Outcome variables for safety include 1. Frequency and percentage of subjects who had solicited injection site and systemic reactions 2. Frequency of subjects reporting medically attended unsolicited adverse events and serious adverse events and the frequencies of these events

Outcome variables for immunogenicity include 1. Post-vaccination seroprotection rates: the proportion of subjects with HAI titers ( $\geq 1:40$ ) for influenza strains following each vaccination. 2. Post-vaccination geometric mean of anti-HAI titers for influenza strains following each vaccination. 3. Post-vaccination GMTs of anti-pertussis (PT, FHA, PRN, and FIM), tetanus, diphtheria, and pneumococcal antigens..

Data analysis plan: The number of subjects enrolled and their age at enrollment (mean, median, and minimum and maximum), sex, and ethnic origin will be summarized for each group, as well as the number and description of protocol violations.

Continuous variables will be presented by summary statistics (eg, mean and standard deviation for the non-immunogenicity endpoints, and geometric means and their confidence intervals for the immunogenicity endpoints), and categorical variables will be presented by frequency distributions (frequency counts, percentages, and their confidence intervals).

**Progress:** This protocol closed to enrollment with fifteen subjects enrolled during FY06; two subjects in Group 1, and thirteen subjects in Group 2. Twelve subjects completed all study interventions. Three were withdrawn prior to study completion; one left the MAMC area, one parent requested to withdraw and one for non-compliance with study requirements. Six month follow-up visits were completed on eleven subjects; four subjects were considered lost to follow-up after phone contact was unsuccessful and certified letters sent. Data analysis is in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203052	<b>Status:</b> Completed
<b>Title:</b> Improving the Delivery of Influenza Vaccine to Young Children: A Comparison of Two Influenza Vaccine Regimens		
<b>Principal Investigator:</b> COL Mary P. Fairchok, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Janet A. Englund, M.D.; Kathleen M. Neuzil, M.D., M.P.H.		
<b>Start - Completion:</b> 4/21/2003 - Mar 2004	<b>Funding:</b> Dr. Englund (UW) via Proffer	<b>Periodic Review:</b> 3/22/2005

**Study Objective:** To compare reactogenicity and immunogenicity of two different dosing regimens of standard licensed trivalent inactivated influenza virus vaccines (TIV) in healthy young children ages 6-23 months.

**Technical Approach:** This is a prospective, randomized, open-label clinical trial comparing reactogenicity and Immunogenicity of two different dosing regimens of standard licensed trivalent inactivated influenza (TIV) vaccines in healthy young children ages 6-23 months. Approximately 150 patients will be enrolled here at MAMC. Patients will be randomized to either the "standard" or the "early" dosing schedules. Both groups will receive two doses of licensed influenza vaccine (TIV) in the fall. However the "early" group will receive an additional dose of the licensed TIV at the time of enrollment. Antibody responses following the two doses of the vaccine in the fall (standard group) will be compared with antibody responses following one dose of vaccine in the spring and a second dose in the fall (early group). A diary of the injection site and systemic symptoms and signs for 5 days following the inoculation will be maintained by the parents. A phone call will be made to the parent beginning three days after the immunization to verify reactions and solicit adverse experiences. Blood samples will be collected at two time points.

**Progress:** This protocol is closed to enrollment, with 126 subjects consented; 117 received at least one Fluzone vaccine as part of the study procedures. Out of 117 subjects, 84 were contacted and six month follow-up information was obtained with no adverse events reported. Following failed phone contact attempts and return/nonresponse to certified letters, 33 subjects were lost to follow-up for the scheduled six month follow-up. The six month follow-up data was submitted for analysis. Final results are pending.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205137	<b>Status:</b> Terminated
<b>Title:</b> Safety and Immunogenicity of Fluzone® Influenza Virus Vaccine (2005-2006 Formulation) Among Healthy Children 6 to 12 Weeks of Age		
<b>Principal Investigator:</b> COL Mary P. Fairchok, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Sue E. Chambers, RN		
<b>Start - Completion:</b> 1/24/2006 - Sep 2006	<b>Funding:</b> Sanofi Aventis via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To demonstrate the safety of Fluzone vaccine administered to 2-month-old children

**Technical Approach:** This is a multicenter, double-blinded placebo controlled trial to compare the safety and immunogenicity of Fluzone® vaccine among healthy children aged 6 to 12 weeks of age at enrollment who are given Fluzone vaccine plus concomitant vaccines versus control children given placebo plus concomitant vaccines. The investigational group (Group 1) will consist of up to 60 subjects enrolled at MAMC. The control group (Group 2) will consist of up to 30 children enrolled at MAMC. Subjects will be randomized to the investigational or control group at a ratio of 2:1. All participants will be enrolled after obtaining informed consent from their parent or guardian.

At study visit 1, Group 1 participants will receive one 0.25 mL intramuscular injection of Fluzone® in addition to the routinely recommended concomitant vaccines of DAPTACEL, ActHIB and Prevnar. Group 1 participants will also receive the routinely recommended Hepatitis B vaccine and Inactivated polio vaccine at either the first study visit, the second study visit, or any time between the 2 study visits that is at least 7 days apart from a study visit. At study visit 1, Group 2 participants will receive one .25ml intramuscular injection of saline placebo in addition to the routinely recommended concomitant vaccines of DAPTACEL, ActHIB and Prevnar. Group 2 participants will also receive the routinely recommended Hepatitis B vaccine and Inactivated polio vaccine at either the first study visit, the second study visit, or any time between the 2 study visits that is at least 7 days apart from a study visit. Both groups will be provided with a diary card to take home at this visit, recording solicited and unsolicited local and systemic adverse effects of the vaccines as well as daily temperatures for the 7 days after the visit.

At study visit 2, Group 1 will receive a second 0.25ml intramuscular injection of Fluzone® in addition to Inactivated polio vaccine and/or Hepatitis B vaccine in the opposite thigh if not previously given. Group 2 will receive a second 0.25 ml intramuscular injection of saline placebo in addition to Inactivated polio vaccine and/or Hepatitis B vaccine in the opposite thigh if not previously given. Interim histories and diary cards will be collected and a second diary card will be provided.

At study visit 3, a blood sample will be collected from all subjects. Diary cards and interim history will be obtained. All subjects will then receive the routinely recommended childhood vaccines of DAPTACEL, ActHIB, Prevnar and Inactivated polio vaccine.

At study visit 4, a blood specimen will be collected from all subjects. There will be a follow up contact by phone of all study participants at 6 months after visit 2 to solicit adverse events.

Outcome variables for safety include 1.frequency and percentage of subjects who had solicited

injection site and systemic reactions. 2. Frequency of subjects reporting any unsolicited adverse events and serious adverse events and the frequencies of these events. 3. Immediate reactions, serious adverse events and adverse events in participants who withdraw due to an adverse event.

Outcome variables for immunogenicity include 1. Geometric mean of anti-HI titers (GMT) following the second of two Fluzone vaccinations given approximately one month apart  
2. Seroprotection rate: The proportion of subjects with seroprotective titer to influenza or concomitant vaccines.

Data analysis plan: Descriptions of the populations will be presented. The number of subjects enrolled and their age at enrollment (mean, median, and minimum and maximum), sex, and ethnic origin will be summarized for each group, as well as the number and description of protocol violations. Continuous variables will be presented by summary statistics (eg, mean and standard deviation for the non-immunogenicity endpoints, and geometric means and their confidence intervals for the immunogenicity endpoints), and categorical variables will be presented by frequency distributions (frequency counts, percentages, and their confidence intervals).

**Progress:** The PI reported the protocol terminated at MAMC 1 February 2006, due to the sponsor meeting enrollment. CRADA/SOW approval was received 25 January 2006, which was not in time to initiate enrollment of MAMC subjects.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205034	<b>Status:</b> Completed
<b>Title:</b> Safety and Immunogenicity of Influenza Virus Vaccine Fluzone® 2004-2005 Among Healthy Children 2 Months vs 6 Months of Age		
<b>Principal Investigator:</b> COL Mary P. Fairchok, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Janet A. Englund, M.D.; Sue E. Chambers, RN		
<b>Start - Completion:</b> 4/18/2005 - Jan 2006	<b>Funding:</b> Aventis Pasteur via University of Washington	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** To determine the safety and immunogenicity of the inactivated influenza vaccine (Fluzone) in healthy children 2 months of age compared to a control group of 6 month olds

**Technical Approach:** This is a multicenter, open label, double-arm, observational and descriptive study that will provide preliminary comparative information about the safety and immunogenicity of Fluzone® vaccine among children aged 6 to 12 weeks (the investigational group) versus children aged 24 to 36 weeks (the control group). The study is not designed to achieve any preset statistical power, and no hypotheses will be tested. At MAMC, we anticipate enrolling a total of 100 patients with 50 infants enrolled in the investigational group and 50 enrolled in the control group. Study participants will receive one 0.25 mL intramuscular injection of Fluzone® at the time of enrollment. A blood specimen will be collected at that visit, and a 7 day diary card will be provided to record any adverse events as well as daily temperatures for the 7 days following the immunization. At visit 2, 21-35 days following enrollment, a second intramuscular injection of 0.25 mL of Fluzone® will be given, interim history and the first diary will be collected and another diary card provided. At Visit 3, 21-35 days after Visit 2, a second blood specimen will be collected, interim history and the second diary card will also be collected. A 6 month followup visit will be conducted on day 210-240 following enrollment at which time an interim history will be obtained. Outcome variables include a comparison of mean geometric titers in each study group against the three components of the influenza vaccine pre and post vaccination, a comparison of the seroprotection and seroconversion rates in each group against each of the 3 components of the vaccine, and record of adverse events after each vaccine. Data analysis: The number of subjects enrolled and their age at enrollment (mean, median, and minimum and maximum), sex, and ethnic origin will be summarized for each group, as well as the number and description of protocol violations. Continuous variables will be presented by summary statistics (eg, mean and standard deviation for the non-immunogenicity endpoints, and geometric means and their confidence intervals for the immunogenicity endpoints), and categorical variables will be presented by frequency distributions (frequency counts, percentages, and their confidence intervals. Additionally, the frequency and percentage of subjects who had solicited local and systemic reactions and their 95% two-sided exact confidence intervals will be calculated. Also, the frequency of subjects reporting medically attended unsolicited adverse events and serious adverse events and the frequencies of these events will be calculated.

**Progress:** This protocol was reported completed in July 2006; final site visit has been conducted by the study sponsor. A total of 40 patients enrolled at MAMC in FY 2005 (May-Jul); 38 received all study treatment/procedures, two patients withdrew after Visit 1: both received 1 dose of Fluzone and blood draw. Reason for withdraw: one patient: moved from state related to parent deployment and one patient self withdrew after serious adverse event (fever presented at ER and hospitalized for R/O sepsis). This adverse event was reported to the IRB and resulted in a revision of the informed consent document.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205139	<b>Status:</b> Ongoing
<b>Title:</b> The Impact of Human Metapneumovirus Versus other Common Respiratory Viruses in Infants in Fulltime Daycare		
<b>Principal Investigator:</b> COL Mary P. Fairchok, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Sue E. Chambers, RN; Melinda L. Behrens, MD; MAJ Loranee E. Braun, MC; Janet Englund, MD		
<b>Start - Completion:</b> 1/25/2006 - Oct 2006	<b>Funding:</b> UW via The Geneva Foundation	<b>Periodic Review:</b> 9/26/2006

**Study Objective:** To determine the impact of common respiratory viruses on infants attending fulltime daycare. Specific objectives include the comparison of duration, lost days from daycare, complications and incidence of the viruses studied in this population.

**Technical Approach:** We will be performing a prospective descriptive study on the duration, clinical characteristics, lost days from daycare, complications and incidence of the viruses studied, with particular attention to the comparison of these characteristics of HMPV infection relative to the other viruses studied. We will conduct rolling enrollment up to 125 subjects/month attending at least 20 hours of daycare per week at one of the Fort Lewis Daycare Centers. Subjects enrolled will be 6 weeks-24 months on enrollment. We will obtain baseline enrollment clinical and demographic data and we will then follow-up with all subjects via mailers or telephone calls on a monthly basis, as well as with notices posted at the daycare, to determine presence of development of acute upper respiratory tract infections. If any 2 out of our 5 defined symptoms for respiratory tract infection should develop, subjects will be given a study visit. At that visit, a standardized health questionnaire will be completed, and a nasal swab for reverse transcriptase pcr for Respiratory Syncytial Virus, Human Metapneumovirus, Parainfluenza 1,2,3 and 4, rhinovirus, coronavirus, influenza A and B viruses, and adenovirus will be obtained. A separate clinical visit with a health care provider will be provided if additional assessment and intervention is necessary. Any positive pcrs would then undergo quantitative assay. Parents will be provided with a diary to complete and mail back recording symptoms and duration of the illness as well as impact on work and daycare. Parents will be called for any positive pcr results and given further information about the virus identified. All subjects will be followed from the time of enrollment until 31 October 2006 unless disenrolled. Outcome variables include the incidence of acute upper respiratory tract infections attributable to HPMV versus the other study viruses in the population, attack rate of each virus in the daycare per month, characteristics of the viral infections, impact on the family in days missed from work or daycare, and duration of infection. Co-infection with other respiratory pathogens and secondary infections will also be recorded. Method of analysis of these variables will be conducted using descriptive statistics

**Progress:** This protocol remains open to enrollment, with 54 subjects enrolled during FY06. Ten patients have been withdrawn; five for ineligibility (removed from daycare) and five moved out of the Fort Lewis area. The remaining 44 subjects are receiving ongoing study treatment per protocol. Presently 83 daycare visits, 48 health care provider visits, and 131 swabs have been performed.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206035	<b>Status:</b> Ongoing
<b>Title:</b> Military Children at Risk - Enhancing Quality of Life (mCARE) Needs Assessment		
<b>Principal Investigator:</b> Karen L. Fitzgerald, RN, PhD		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Janice L. Hansen, PhD; Virginia F. Randall; Jason P. Cervenka		
<b>Start - Completion:</b> 12/20/2005 - Dec 2006	<b>Funding:</b> TATRC via MIPR	<b>Periodic Review:</b> N/A

**Study Objective:** To delineate the needs of children with life-threatening illnesses and their families who are eligible for care in the Military Health System (MHS). To delineate the educational needs of pediatricians (pediatric residents, general pediatricians and pediatric sub-specialists) that relate to providing and coordinating care for children with life threatening illnesses and their families. To analyze the TRICARE benefit and services provided by the MHS in relation to the needs of children with life threatening illnesses and their families. To develop recommendations for a program to provide health care services to military children with life threatening illnesses and their families.

**Technical Approach:** This is Phase II of a needs assessment of military families with children with life-threatening illnesses, using a case study methodology. Phase II will include case studies of the areas surrounding the Madigan AMC, Naval Medical Center, San Diego Munson AHC at Ft. Leavenworth, KS. Altogether, there will be case studies of the National Capitol Area (NCA), areas surrounding installations with major medical centers, and the area surrounding a small installation with limited services available through the direct-care MHS. Data collection will include interviews and/or focus groups with parents, interviews and focus groups with health care providers, and collection of TRICARE data regarding case management and utilization of care. Three existing surveys (the FACCT End-of-Life Survey, Medical Home Assessment Tools, and a survey of the quality of life of caregivers previously developed by the investigators with parent advisors) will provide the basis for interview and focus group questions. Needs identified will be compared to the services available at each site and then to the services covered by the TRICARE benefit. In collaboration with other partners in the mCARE project, needs identified by parents of children with life-threatening illnesses and health care providers who provide care for them will be compared to services provided by the MHS, the TRICARE benefit, and community resources. The assessment will also describe access and barriers to access for services from these three sources. Subsequently, the mCARE project team will propose a model of care for military children and their families that will provide a coordinated, comprehensive, family-centered approach to care from the time of diagnosis of a life-threatening illness through the time of bereavement of families. This proposal also adds the following components to the needs assessment: development of an advisory group of parents in the NCA, a collaboration with Family Medicine, adaptation to this population of a previously-developed measure of quality of life of caregivers, technical assistance in defining eligibility criteria, and participation in evaluation of program components piloted by other mCARE project team members (respite care and/or care coordination).

**Progress:** During 2006, data was gathered from MAMC, San Diego Naval Medical Center, Wright-Patterson Medical Center, and within the NCA. Overall 100 health care providers and 93 parents enrolled; of these participants, 28 health care providers and 35 parents were from MAMC. Analysis of parent transcripts from the NCA has yielded a preliminary list of themes, which has begun to identify the needs of families and the difficulties they face. Analysis of health care provider transcripts from NCA and MAMC has yielded a separate preliminary list of themes, which has also begun to identify the needs of health care providers themselves and those they recognize facing the families they see.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205065	<b>Status:</b> Ongoing
<b>Title:</b> Staphylococcus Aureus Intestinal Colonization Among Healthy Infants		
<b>Principal Investigator:</b> LTC Dolores M. Gries, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Curtis J. Donskey, M.D.; CPT Tamatha F. Zemzars, MC; CPT Katy J. Gibson, MC; Meera R. Iyer, M.D.; MAJ Steven D. Mahlen, MS; Mary L. Myers, MT; CPT Elisa D. O'Hern, MC		
<b>Start - Completion:</b> 7/19/2005 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4/25/2006

**Study Objective:** (1) To perform a prospective survey to examine the incidence and density of *S. aureus* carriage among healthy infants. (2) To evaluate whether infants with increased density of *S. aureus* in stool have increased frequency of environmental and skin contamination. (3) To examine the molecular epidemiology of *S. aureus* isolates among healthy infants and their mothers. (4) To determine the potential for MRSA and other nosocomial pathogens to grow in stool of healthy infants. (5) To determine the incidence of *S. aureus* infection in healthy colonized infants during the first 2 weeks of life.

**Technical Approach:** A 12-month prospective study will be conducted in the MAMC Newborn Unit and Well Child Clinic. Cultures of anterior nares, skin, discarded stool, and environmental surfaces in the room of infants will be obtained. Cultures of the anterior nares of the mother will be obtained. Samples will be analyzed for the presence of MSSA or MRSA. Stool samples will be evaluated for the ability of MRSA and other important nosocomial pathogens to grow in stool specimens. Molecular typing using pulsed-field gel electrophoresis will be performed at the Cleveland VA Medical Center to identify the potential source of the bacteria.

**Progress:** This protocol remains open to enrollment with thirteen patients enrolled at MAMC. The incidence of staph colonization thus far remains at approximately 15%. No MRSA has been found. Enrollment and follow-up remains ongoing.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 204097	<b>Status:</b> Terminated
<b>Title:</b> Effect of Immunomodulatory Diet Upon 5-Fluorouracil Induced Oral and Intestinal Mucositis in Golden Syrian Hamsters (Mesocricetus auratus)			
<b>Principal Investigator:</b> CPT Wendy T. Harsha, MC			
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Wayne J. Harsha, MC; CPT Ellina Kalandarova, MC; COL James M. Noel, Jr., MC; LTC Robert G. Irwin, MC; CPT Patrick M. McNutt, MS; CPT Roy F. Thomas, MC			
<b>Start - Completion:</b> 8/11/2004 - Jul 2007		<b>Funding:</b> Society of Military Otolaryngologists Research Grant via T.R.U.E	<b>Periodic Review:</b> 8/10/2005

**Study Objective:** Cancer chemotherapy often causes damage to the lining of the mouth and gut, known as mucositis. When mucositis occurs in the mouth and throat, the patients suffer from painful ulcerations that limit their ability to talk and eat. Additionally, mucositis in the gut predisposes patients to secondary problems such as infections, nausea, vomiting and malnutrition. A number of growth factors and cytokines (signaling molecules of the body) have been implicated in intestinal and oral regeneration in various animal models involving mucositis. These factors include glutamine, transforming growth factors alpha and beta, insulin-like growth factor, and other cytokines. It is possible to reproduce intestinal and oral mucositis in laboratory animals with systemic injections of 5-Fluorouracil (5-FU).

**Technical Approach:** The aim is to address the 5-FU induced damage to the oral and gastrointestinal tract of hamsters. The hamsters will be fed either a standard diet or a polymeric formula containing glutamine, transforming growth beta (TGF-Beta) and short chain fatty acids (SCFAs). Objective and semi-objective measurements of oral ulceration will be evaluated daily and, after sacrifice, both the oral and gastrointestinal mucosa will be evaluated by an objective pathologist who is unaware of the groups from which the samples came. In addition, during the study we will measure nutrition parameters to include daily weights, albumin levels and bicarbonate levels.

**Progress:** We completed both the pilot portion of the protocol and the first phase of study hamsters. We made some changes to the protocol based on results seen in the pilot study then proceeded with the first phase of study hamsters. In the 42 study hamsters, the preliminary statistics show that the study hamsters showed improved weight and food intake versus the control animals. The GI data is still in the process of being analyzed, and the BrDU data is still waiting to be run. The cheek pouch data has shown a trend toward improvement in the study animals.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206021	<b>Status:</b> Ongoing
<b>Title:</b> EKG Screening in ROTC Cadets; Is It Useful?		
<b>Principal Investigator:</b> CPT Erik R. Johnson, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Mark J. Devenport, MC; LTC Robert A. Puntel, MC; LTC Telita Crosland, MC; MAJ Victoria W. Cartwright, MC; MAJ John A. Edwards, MC		
<b>Start - Completion:</b> 11/30/2005 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To determine how often screening electrocardiograms (EKG's) in ROTC cadets disclose abnormal EKG findings, (2) which specific cardiac abnormalities are discovered, (3) what percentage of abnormal screening EKG's disclosed life-threatening or serious cardiac illness that require further consultation and (4) what percentage of cadets are disqualified from entering flight school due to EKG findings and/or further evaluation.

**Technical Approach:** This is a retrospective study designed to have no impact whatsoever on the routine care of the ROTC candidates seen at Ft. Lewis, Washington during the Summer of 2005 as part of Warrior Forge. Each year, approximately 500-700 cadets undergo evaluation for flight status as an additional part of their ROTC experience (current year's estimate is around 600) and receive screening EKGs in addition to other routine medical evaluations. Data [age, sex, height, weight, abnormalities listed on EKG, any consultations or further evaluations made, specifically cardiology referral (yes/no and descriptive clinical findings of referral)] will be obtained and recorded into an Excel spreadsheet database using medical records available (CHCS, ICDB, and Aviation Medicine Clinic medical records available for review). Results of each cadet's flight status (yes/no) will be requested from Aviation Medicine Clinic.

**Progress:** Data analysis completed and abstract sent to USPS, but not accepted. Investigators plan to review this past summer's RPTC EKG records to add more numbers to the data.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203119	<b>Status:</b> Ongoing
<b>Title:</b> Alternating Antipyretics: Antipyretic Efficacy Of Acetaminophen Versus Acetaminophen Alternated With Ibuprofen In Children		
<b>Principal Investigator:</b> CPT Lynne C. Kramer, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Mary P. Fairchok, MC; COL (Ret) Patrick C. Kelly, D.O.; CPT Amy M. Thompson, MC; CPT Peaches A. Richards, MC; CPT Keith R. Compton, MC; CPT David P. Harper, MC		
<b>Start - Completion:</b> 2/27/2004 - Feb 2004	<b>Funding:</b> American Academy of Pediatrics via The Geneva Foundation	<b>Periodic Review:</b> 8/22/2006

**Study Objective:** To compare the antipyretic efficacy of alternating ibuprofen and acetaminophen to acetaminophen alone.

**Technical Approach:** Infants and children 6 months to 6 years meeting inclusion and exclusion criteria who present to the pediatric clinic with a fever of 100.4 or greater will be offered enrollment into the study. Baseline temperature will be recorded and initial dose of acetaminophen will be given. All temperature measurements will be made using a standard oral or rectal thermometer provided by the investigators. Parents will receive a handout and instruction on facts and myths related to fever and fever control in children. Baseline demographic data will be recorded to include age, sex, race, and underlying medical conditions. Parents or caregivers will be trained to take temperature with the study thermometer and administer study medications. Subjects will be randomized via computer based random number to either the acetaminophen group or the acetaminophen/ ibuprofen group. Group selection will be unblinded only to the co-investigator entering the study medications into CHCS. Study medications will include acetaminophen, ibuprofen, and placebos designed to mimic ibuprofen and acetaminophen. Each patient will receive a study medication or placebo at time zero, 3 hours and 4 hours. Acetaminophen group will receive acetaminophen time zero, placebo time 3 hours and acetaminophen time 4 hours. Acetaminophen + ibuprofen group will receive acetaminophen time zero, ibuprofen time 3 hours and placebo time 4 hours.

Temperatures will be obtained and recorded from each subject at 0, 3, 4, 5 and 6 hours. The study will end at 6 hours. All subjects will receive standard of care for their presenting complaints. The study will not interfere with the evaluation or treatment of these complaints. Once the medical evaluation for the presenting complaint is complete subjects will be sent home or admitted depending on their medical condition. For subjects at home, the parent or caretaker will complete the study. A study investigator will contact the parent or caretaker at 6 hours and obtain the results. At the conclusion of the study period, parents will read the provided instruction sheet on what further antipyretics and antipyretic schedule may be administered to the child in the case of continuing fever. The information will be provided as a sealed instruction sheet matched to the randomized group, so that the study investigator will remain blinded.

**Progress:** This protocol is closed to enrollment with 38 subjects enrolled; eleven in the last year. Follow-up is complete and data analysis is underway with efforts to produce a manuscript by the end of August 2006.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205110	<b>Status:</b> Ongoing
<b>Title:</b> AALL03N1, Understanding the Ethnic and Racial Differences in Survival in Children with Acute Lymphoblastic Leukemia		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 11/17/2005 - May 2008	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 7/10/2006

**Study Objective:** (1) To determine and compare adherence to 6-MP in a cohort of children with ALL from four different ethnic and racial groups (Caucasians, African-Americans, Hispanics, and Asians) receiving maintenance chemotherapy, using the following assessments: serial red cell 6-MP metabolites (6TGN and MethylTIMP), frequency of 6-MP dosing using an electronic pill monitoring system (MEMS®), and self-report of adherence to 6-MP by questionnaire. (2) To determine the impact of adherence to 6-MP (measured using 6TGN, MeTIMP, MEMS® and self-report data independently) on event-free-survival (EFS) in the entire cohort, after adjusting for known predictors of disease outcome. (3) Define a critical level of adherence (measured independently by 6TGN, MeTIMP, MEMS®, self-report) that has a significant impact on EFS for the entire cohort. (4) Describe prevalence of adherence to 6-MP by ethnicity (6TGN, MeTIMP, MEMS®, Selfreport). (5) Describe behavioral and socio-demographic predictors of adherence using the questionnaire data. (6) Describe the pill-taking practices in this cohort using the MEMS® data. (7) To evaluate the impact of adherence on ethnic/racial difference in EFS. (8) To assess the concordance among 6TGN and MeTIMP levels, electronic pill monitoring, and self-reported adherence in the ethnic/racial groups.

**Technical Approach:** This study will assess adherence to 6-MP in a cohort of children with ALL from four different ethnic and racial groups (Caucasians, African-Americans, Hispanics, and Asians), who are receiving maintenance chemotherapy, by measuring red cell 6-MP metabolites (6TGN, MethylTIMP), frequency of 6-MP dosing using an electronic pill monitoring system (MEMS), and self/care-giver report of adherence to 6-MP. Participants will be asked to provide 5 ml blood samples during 7 time points and complete an adherence questionnaire at 4 time points during their regularly scheduled clinic appointments. Blood samples will be used for analysis of genetic polymorphisms related to the efficacy of anti-leukemic therapy, and measurement of red cell 6TGN/TIMP levels (eg. TPMT). Participants will also be given an electronic cap to use with their 6-MP medication bottle that will record the date and time of bottle opening. The COG anticipates about 720 patients less than or equal to 21years of age will be participating in this study. The enrollment for MAMC is estimated to be 2-3 patients per year.

**Progress:** This protocol remains open to enrollment with no patients enrolled.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206052	<b>Status:</b> Ongoing
<b>Title:</b> ACNS0331 A Study Evaluating Limited Target Volume Boost Irradiation and Reduced Dose Craniospinal Radiotherapy (18.00 Gy) and Chemotherapy in Children with Newly Diagnosed Standard Risk Medulloblastoma: A Phase III Double Randomized Trial		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Joseph P. Brooks, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 3/30/2006 - Oct 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary Objective: To determine whether reducing the craniospinal dose of radiation therapy to 18.00 Gy in children 3-7 years of age does not compromise event-free survival and overall survival as compared to treatment with 23.40 Gy of craniospinal radiation; and to determine if reducing the irradiated volume of the primary site tumor boost from the whole posterior fossa to the tumor bed only will not compromise event-free and overall survival.

Secondary Objectives: To evaluate patterns of failure in children treated with an irradiation boost volume smaller than conventional posterior fossa volumes. To reduce the cognitive, auditory and endocrinologic effects of treatment of average-risk medulloblastoma by reducing the dose of craniospinal irradiation therapy. To determine if the audiologic and endocrinologic toxicity will be reduced with the use of limited tumor boost volume irradiation compared to patients treated with conventional target volumes of radiation. To develop an optimal gene expression medulloblastoma outcome predictor, validated prospectively in a multi-institution randomized clinical trial. To improve compliance with long-term quality of life and functional status data submission by educating institutional nurses to administer and submit for analysis a battery of four instruments: Behavior Assessment System for Children (BASC), Adaptive Behavior Assessment System (ABAS), Behavior Rating Inventory of Executive Function (Brief), PedsQLTM 4.0.

**Technical Approach:** In order to compare the effects of different doses and volumes of radiation, children will be randomized to radiation treatment plans at the time of study entry. Children ages 3 and less than age 8 will be randomized twice. They will be randomized between two doses of craniospinal radiation and between a standard volume boost and a smaller volume boost. All children 8 years and older will be given the standard dose of craniospinal radiation and will only be randomized for the boost volume of radiation. Chemoradiotherapy begins about 4 weeks after surgery. Radiation therapy to the brain and spine will be given 5 days each week for 6 weeks. Vincristine will be given IV push once a week for 6 weeks beginning at Week 1 (one week after the start of radiation). Maintenance Chemotherapy begins 4 weeks after the completion of chemoradiotherapy. There will be 9 cycles of maintenance; two different kinds of cycles given. Cycle A lasts for 6 weeks and Cycle B for 4 weeks (given after the completion of 2 A cycles).

**Progress:** This protocol is open to patient entry, with no patients enrolled during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206095	<b>Status:</b> Ongoing
<b>Title:</b> AEWS02B1, A Group wide Biology and Banking Study for Ewing Sarcoma		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 7/26/2006 - May 2016	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Objectives: (1) To develop a mechanism to collect and distribute tumor specimens to various investigators, and a system to prioritize and develop quality-control measures for central data reporting of studies undertaken. (2) To determine the prognostic significance of translocation subtype in Ewing sarcoma; to determine the prognostic significance of translocation negative Ewing sarcoma. (3) To determine the prognostic significance of MRD detection in bone marrow specimens by RT-PCR determination of EWS-ETS fusion genes. (3) To determine whether serum levels of IGF1, IGFBP3 are of significance in the outcome of patients with Ewing sarcoma. (4) To determine whether RNA expression profiles performed on diagnostic specimens will allow for the identification of newer prognostic categories and potentially new molecular targets for treatment in Ewing sarcoma. (5) To identify new treatment targets for therapy. Further testing of these potential targets will be carried out in hopes of expediting translation of these findings to the clinic. (6) To establish a bank of Ewing sarcoma xenografts in SCID/Beige mice. (7) To establish clinical proteomics as a resource for investigations of altered signaling molecules in the pathogenesis of Ewing sarcoma.

**Technical Approach:** Study AEWS02B1 is a biology and banking study for Ewing Sarcoma designed to analyze biological factors of Ewing's tumors and relate tumor characteristics to treatment outcomes. At initial diagnosis extra tumor specimens will be sent to the Children's Oncology Group (paraffin blocks or unstained slides and thick sections, blood, bone marrow, serum, fresh sterile tumor frozen in OCT media, and fresh sterile tumor in RPMI). Pathologists are encouraged to submit additional tumor tissue obtained at the time of later biopsies or surgical procedures to document response, recurrence, or progressive disease, and tissue obtained at autopsy. Enrollment for MAMC is estimated to be 1-2 patients per year.

**Progress:** This protocol remains open to patient entry, with no patients enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206096	<b>Status:</b> Ongoing
<b>Title:</b> AHOD0431, A Phase III Study for the Treatment of Children and Adolescents with Newly Diagnosed Low Risk Hodgkin Disease		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 8/11/2006 - Feb 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Objectives: (1) To investigate the paradigm of response-based therapy for low risk Hodgkin disease by eliminating involved-field radiation therapy (IFRT) for subjects who achieve a CR with initial chemotherapy. (2) To investigate whether three cycles of AV-PC\* for the treatment of low risk Hodgkin disease is sufficient to induce CR in at least 80% of subjects. (3) To investigate whether subjects who experience a low risk relapse after initial treatment with chemotherapy alone can be successfully treated with a salvage regimen consisting of IV/DECA and IFRT. (3) To maintain the overall survival (OS) for subjects with low risk Hodgkin disease at or above 97%. (4) To determine the prognostic significance of very early response as measured by FDG-PET or gallium after the first course of chemotherapy. (5) To evaluate the prognostic significance of elevation of ESR and CRP at the time of diagnosis in low risk Hodgkin disease on CR rate and relapse rate after chemotherapy alone. (6) To determine the frequency and severity of late effects of therapy including thyroid dysfunction, infertility, cardiotoxicity and second malignant neoplasms.

**Technical Approach:** All patients will have initial treatment utilizing AV-PC\* with or without involved field radiation therapy. Those patients who are in complete remission after three cycles of AV-PC\* will begin follow-up. Those patients who are in partial remission after three cycles will receive involved field radiation therapy. Those who fail to achieve a partial remission with initial chemotherapy, who have progressive disease prior to completing initial therapy, or who fail to achieve a complete remission after radiation therapy will be off study. All patients with a positive FDG-PET (or gallium) prior to initiating treatment will have a second scan after one course of AV-PC\* utilizing the same modality as the initial scan (FDG-PET strongly encouraged if available). Those with a persistently positive study will have a third scan after chemotherapy to document remission status. Patients who experience a biopsy proven low risk recurrence after achieving a complete remission with chemotherapy alone will be treated with a salvage regimen. The initial treatment will consist of 3 cycles of AV-PC\*. Each cycle is 21 days in duration and commences on Day 1 if the ANC > 750 (with patients off G-CSF for at least 2 days) and platelets are > 75,000. Subjects in complete remission after three courses of initial chemotherapy will stop treatment and begin follow-up. Subjects with partial remission after three courses of initial chemotherapy will proceed to involved field radiation therapy. Radiation therapy will commence approximately 4 weeks after the 3rd cycle of AV-PC\* is completed and when ANC >1000 and platelet count >100,000. Patients who experience a biopsy proven low risk relapse after achieving a complete remission with chemotherapy alone at initial treatment, and therefore have not had prior radiation therapy, will be treated with two cycles of Ifosfamide and Vinorelbine, followed by two cycles of Dexamethasone, Etoposide, Cisplatin, ARA-C followed by involved field radiation therapy. Each cycle will be 21 days in length. All relapses must be biopsy proven. All patients on the salvage regimen will proceed to involved field radiation therapy after four cycles of salvage chemotherapy. Radiation therapy will commence approximately 4 weeks after the 2nd cycle of DECA is completed and when ANC >1000 and platelet count >100,000.

**Progress:** This protocol remains open to patient entry, with no patients enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206051	<b>Status:</b> Ongoing
<b>Title:</b> ANBL0032 Phase III Randomized Study Of Chimeric Antibody 14.18 (Ch14.18) In High Risk Neuroblastoma Following Myeloablative Therapy And Autologous Stem Cell Rescue		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 4/6/2006 - Oct 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objective to determine if monoclonal antibody Ch14.18 + cytokines + isotretinoin (13-cis-retinoic acid, or RA) improves event free survival after myeloablative therapy and stem cell rescue as compared to RA alone, in high risk neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR.

Secondary objectives: (1) to determine if monoclonal antibody Ch14.18 + cytokines + isotretinoin (13-cis-retinoic acid, or RA) improves overall survival after myeloablative therapy and stem cell rescue as compared to RA alone, in high risk neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR. (2) Determine if immunotherapy + RA improve event free survival and overall survival as compared to RA alone, in the subgroup of high risk INSS stage 4 neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR. (3) To determine the variability of 13-cis-retinoic-acid pharmacokinetics and relationship to pharmacogenomic parameters and determine if these levels and/or genetic variations correlate with EFS or systemic toxicity. (4) In the subgroup of neuroblastoma patients who have achieved a pre-ASCT response of CR, VGPR, or PR, determine if there is a difference between the two randomized regimens in reducing the minimal residual disease (MRD) burden as detected by the following parameters: meta-iodobenzylguanidine (MIBG) scan, immunocytology (IC) of blood and bone marrow samples, RT-PCR for tyrosine hydroxylase, PGP 9.5, and MAGE-1 in blood and bone marrow. (5) Determine if change from baseline of MRD as measured by above parameters is associated with event free and overall survival. (6) Determine whether tumor biology at diagnosis correlates with event-free and overall survival, for either of the randomized regimens. (7) Determine the toxicities of the combination of monoclonal Ch14.18 with cytokines. (8) To explore the relationship between antibody-dependent cellular cytotoxicity (ADCC) and EFS. (9) To determine a descriptive profile of human anti-chimeric antibody (HACA) during immunotherapy. (10) To compare the outcome data of the patients with persistent disease documented by biopsy (stratum 07) to the historical data for the analogous patients from CCG-3981.

**Technical Approach:** Patients will be enrolled and randomized into regimen A or B on day 50 post-ASCT, up to day 77 (see special exemption) post-ASCT when 1) total absolute phagocyte count (APC) is at least 1000/?L 2) organ functions have met the eligibility criteria, and, 3) tumor assessment has been completed following the end of radiotherapy at least 5 days before.

Randomization will be stratified by pre-ASCT CR versus VGPR versus PR and by purging vs. nonpurging of the stem cells for ASCT. Regimen A consists of oral intake of isotretinoin (13-cis-retinoic acid, or RA) starting day 66 post-ASCT at 80 mg/m<sup>2</sup>/dose twice a day for 14 days every 28 days, for 6 courses. For regimen B, patients will receive oral isotretinoin (13-cis-retinoic acid, or RA) as in regimen A. In addition, patients will receive 5 courses of ch14.18 + cytokines, with ch14.18 + GM-CSF administered in courses 1, 3, and 5, and ch14.18 + aldesleukin (IL-2) given in courses 2 and 4. The intervals between antibody administrations are 28 days for all courses.

**Progress:** This protocol is open to patient entry, with no patients enrolled during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206097	<b>Status:</b> Ongoing
<b>Title:</b> AREN03B2; Renal Tumors Classification, Biology, and Banking Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 7/26/2006 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To classify patients with renal tumors by histological categorization, surgical-pathological stage, presence of metastases, age at diagnosis, tumor weight and loss of heterozygosity for chromosomes 1p and 16q, to thereby define eligibility for a series of therapeutic studies. To maintain a biological samples bank to make specimens available to scientists to evaluate additional potential biological prognostic variables and for the conduct of other research by scientists.

**Technical Approach:** This classification protocol will provide the mechanism to identify renal tumor patients on a population basis, and to describe their characteristics at diagnosis. This study will also establish the natural history (relapse-free and overall survival) for patients with disease for which there will not be a therapeutic or outcomes study (all renal tumors except Wilms, rhabdoid, clear cell sarcoma, and renal cell carcinoma). These cases, after central review results are reported back to the enrolling Institution, will be followed (date of last follow-up, relapse, and death) as part of their enrollment on AREN03B2. It is expected that all such patients, even with benign tumor, will be followed at least yearly, for a period of about ten years, by the enrolling Institution (at the time of enrollment, institutions will be notified which cases must be followed). Patients less than 30 years of age will be participating in this study. The enrollment for MAMC is estimated to be 1-2 patients per year.

**Progress:** This protocol is open to patient entry, with one patient enrolled at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 200032	<b>Status:</b> Completed
<b>Title:</b> COG 9900, ALinC 17, Classification (C), B-Precursor Induction Treatment (I) Protocol			
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC			
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC			
<b>Start - Completion:</b> 1/25/2000 - Jan 2005		<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 12/8/2005

**Study Objective:** (1) To provide the clinical and laboratory data necessary for placing each patient with ALL onto proper therapeutic trial, and (2) to provide an administrative base to capture classification data for correlative studies in ALL treatment protocols and series of historical protocols.

**Technical Approach:** At the time of diagnostic evaluation which includes bone marrow aspiration and/or biopsy, 20 ml of bone marrow and 25 ml of peripheral blood will be collected and processed for local laboratory studies and submission to the following POG reference laboratories: 1. Johns Hopkins University for Immunophenotyping. 2. University of New Mexico (UNM) for DNA Index, FISH, Molecular testing, Cell banking. 3. Medical College of Wisconsin for Glucocorticoid receptors. 4. University of Texas Southwestern Medical Center for Homocysteine Children's Hospital of Michigan for Drug sensitivity profiles. 5. MUSC - Children's Hospital for Drug sensitivity profiles. UCSD Medical Center for Tumor suppressor gene studies. The data captured on this protocol will be used in the therapeutic trials, in cross era analysis, and in international collaborations to further define the prognostic importance of biologic features in ALL.

**Progress:** This protocol was reported as completed in August 2006, with eleven patients enrolled at MAMC, none during FY06. One patient is deceased and the other ten patients will continue to be followed under their therapeutic protocols.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200077	<b>Status:</b> Ongoing
<b>Title:</b> COG 9904, ALinC 17: Treatment for Patients with Low Risk Acute Lymphoblastic Leukemia, A Phase III Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 5/12/2000 - May 2004	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 4/25/2006

**Study Objective:** (1) In conjunction with POG 9905, to compare short MTX infusion (2g/m2 over 4 hours) with a longer infusion (1g/m2 over 24 hours), primarily with respect to efficacy and secondarily with respect to toxicity. (2) to determine in a randomized trial, if a delayed multi-drug intensification, administered in the context of intensive anti-metabolite therapy, will improve outcome for children with ALL, (3) To determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction), and (4) To determine the relationship between a membrane bound glucocorticoid receptor and EFS via quantitation of the glucocorticoid receptor concentrations in marrow samples at diagnosis.

**Technical Approach:** This protocol will randomize between the 4-hour and 24 hour methotrexate infusion and for patients with TEL/AML1 gene, between standard and delayed intensification. Data from POG 9904 and 9905 will be pooled for statistical analysis of efficacy and toxicity. This study will determine the correlation between peripheral blood and CSF concentrations of homocysteine and its metabolites and acute (seizures) and chronic neurotoxicity (neurocognitive dysfunction). Induction will include three or four drugs (dependent on initial risk classification POG 9900).

**Progress:** This protocol closed to patient entry in April 2005, with four patients enrolled. One patient remains on treatment and three patients have completed study treatment; all continued to be followed at MAMC during FY06.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200139	<b>Status:</b> Ongoing
<b>Title:</b> COG A5971: Randomized Phase III Study for the Treatment of Newly Diagnosed Disseminated Lymphoblastic Lymphoma or Localized Lymphoblastic Lymphoma, A Phase III COG Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 9/26/2000 - Sep 2007	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 8/24/2006

**Study Objective:** (1) To compare the event free survival and survival in patients with disseminated lymphoblastic lymphoma treated on four regimens. (NHL/BFM-95 vs. CCG BFM), (2) To determine if treatment with a regimen without high dose methotrexate will maintain the same excellent disease free survival obtained with NHL/BFM-90, (3) To determine if intensification with anthracycline and cyclophosphamide improves disease free survival, (4) To collect outcome data on uniformly treated patients with localized disease or CNS positive disease, and (5) To determine if rapid reduction in tumor volume as defined by chest radiography and CT is predictive of improved outcome.

**Technical Approach:** Patients with disseminated (Murphy stage III or IV) lymphoblastic lymphoma without evidence of CNS disease will be randomized to one of four treatment regimens: Standard CCG BFM (regimen A1); CCG BFM intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen A2); Standard NHL/BFM-95 (regimen B1); or NHL/BFM-95 intensified with cyclophosphamide/anthracycline intensification during the induction and delayed intensification phases (regimen B2). Patients with disseminated lymphoblastic lymphoma positive for CNS disease will be assigned to the intensified NHL/BFM-95 arm (regimen B2) with delayed radiation therapy. Patients with localized lymphoblastic lymphoma (Murphy stage I or II) will be assigned to the standard CCG BFM arm without additional intrathecal methotrexate (regimen AO). The duration of each treatment arm is 2 years and consists of Induction, Consolidation, Interim Maintenance, Delayed Intensification, and Maintenance therapies.

**Progress:** COG temporarily closed accrual to this protocol in September 2005, to assess whether the number of evaluable patients was sufficient to answer the study question. Madigan had enrolled one patient in 2004, who is currently being treated at WRAMC, although MAMC continues to be responsible for data submission to COG. COG lifted the temporary suspension and the protocol was approved by the IRB to continue patient enrollment at MAMC on 26 September 2006.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205015	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL0031, A COG Pilot Study for the Treatment of Very High Risk Acute Lymphoblastic Leukemia in Children and Adolescents		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 4/5/2005 - Jun 2005	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 10/24/2006

**Study Objective:** Primary Objective: To determine the feasibility in terms of patient accrual and toxicity of an intensified chemotherapeutic regimen incorporating novel agents for treatment of children and adolescents with very high risk (VHR) ALL. Secondary Objectives: (1) To determine if the BCR-ABL-specific tyrosine kinase inhibitor STI571 can be incorporated into this regimen with acceptable toxicity for patients with Ph+ ALL. (2) To compare EFS for VHR patients treated with the intensive chemotherapy with that of historical controls. (3) To conduct a preliminary evaluation of the feasibility and efficacy of following intensive consolidation by Hematopoietic Stem Cell Transplantation (HSCT) as therapy for patients with HLA matched related donors. (4) To determine if MRD assessed at the end of induction and prior to reinduction and prior to HSCT therapy by PCR and flow cytometry can predict relapse. (5) To evaluate whether MRD detected by PCR at post-intensification time points is prognostically significant. (6) To evaluate whether gene expression patterns can be identified by microarray evaluations to predict disease recurrence or response to STI571.

**Technical Approach:** This pilot study will utilize a novel intensified chemotherapeutic regimen for VHR patients based on (1) the use of ifosfamide and etoposide in POG ALL relapse studies; (2) the use of high dose methotrexate for children and infants; and (3) the intensive CCG New York II regimen used for patients with lymphomatous ALL. The study will determine whether an adequate number of VHR patients will be accrued to form the basis for development of a future phase III trial within the COG. The presence or absence of minimal residual disease in patients in remission also will be determined. If the intensive treatment is found to have acceptable toxicity and shows potential, either alone, or with transplant, for improving outcome of the VHR patient population, it will be the first promising strategy identified for this group. The accrual goal is 110 patients over a 2 year time frame.

**Progress:** This protocol closed to accrual in October 2006. MAMC enrolled one patient enrolled who continued to be followed during FY06. The patient is no longer receiving study treatment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205068	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL0232, High Risk B-precursor Acute Lymphoblastic Leukemia		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 7/29/2005 - Mar 2015	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** (1) To improve the outcome of children with high risk acute lymphoblastic leukemia. (2) To determine the relative safety and efficacy of dexamethasone given for 14 days versus prednisone given for 28 days during Induction. (3) To determine the relative safety and efficacy of high dose methotrexate (5gm/m<sup>2</sup>) with Leucovorin rescue compared to escalating methotrexate without Leucovorin rescue (Capizzi I) delivered during Interim Maintenance. (4) To correlate Day 29 Minimal Residual Disease (MRD) with Event Free Survival (EFS) and Overall Survival (OS). (5) To correlate early marrow response status with Day 29 MRD status. (6) To improve outcome by identifying additional high risk patients by day 29 MRD for treatment with fully augmented BFM.

**Technical Approach:** This study will compare the use of two steroid drugs, dexamethasone and prednisone, during induction and will examine the best way to give methotrexate during the interim maintenance phase of treatment. This study will use a known chemotherapy regimen that has been very effective for treating children with high risk ALL and test whether two changes to this treatment can cure more patients without increasing side effects. The aim of the first change is to test whether 14 days of dexamethasone is tolerated without an increased number of severe side effects and is better than 28 days of prednisone in decreasing the number of leukemia cells during the first month of treatment. The aim of the second change is to determine whether giving higher doses of methotrexate, during interim maintenance, will work better than giving it on a schedule that starts with a lower dose and increases with each of the later doses.

**Progress:** This protocol remains open to enrollment with two patients enrolled at MAMC, 1 during FY06. Two patients received study treatment. One patient was an induction failure, was taken off study and enrolled onto another COG protocol.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205095	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL0331, Standard Risk B-precursor Acute Lymphoblastic Leukemia; A Phase III Group-Wide Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 12/15/2005 - July 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** (1) To determine whether the substitution of three intensified phases of post-induction treatment for standard phases will improve the event free survival (EFS) of children with SR-average acute lymphoblastic leukemia (ALL). (2) To determine whether the addition of four doses of PEG Asparaginase, given once every three weeks during consolidation and interim maintenance phases, will improve the EFS for children with SR-low ALL. (3) To identify potentially modifiable factors associated with impaired health related quality of life (HRQOL) at different periods of therapy in the patients who are SR-average enrolled on the standard risk ALL study. (4) To determine the critical time periods when future intervention studies to mitigate adverse HRQOL outcomes should occur. (5) To correlate Day 29 Minimal Residual Disease (MRD) with EFS and Overall Survival (OS). (6) To correlate early marrow response status with Day 29 MRD status. (7) To improve outcome by identifying additional high risk patients by Day 29 MRD for treatment with fully augmented BFM. (8) To examine the relative contributions of genetic factors and early treatment response to outcome by comparing the outcome of patients with and without TEL-AML1 fusion or triple trisomy and low levels of MRD at end Induction who are treated with identical therapy on the standard arms of the SR-low and SR-average trials.

**Technical Approach:** Patients treated on this study will receive multiple drugs all designed to kill leukemia cells. Patients who have an appropriate donor will be given a blood and marrow transplant. Those without an appropriate donor will continue on with more chemotherapy. Patients with high levels of cancer cells in the spinal fluid will also receive radiation to the brain. Boys with leukemia cells in the testes will receive radiation to the testes. Patients receiving a blood and marrow transplant will also be given radiation to the entire body before their transplant and will be hospitalized for about three months during treatment. The new drug for patients with leukemia containing the Philadelphia chromosome positive (Ph+) is called Imatinib (STI571), and it is given throughout treatment. If a patient goes on to have a blood and marrow transplant, Imatinib (STI571) may be given after the transplant at the transplant center or at the primary care center

**Progress:** This protocol remains open to enrollment with one patient enrolled during FY06 and continuing to receive treatment.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205067	<b>Status:</b> Ongoing
<b>Title:</b> COG AALL03B1, Classification of Acute Lymphoblastic Leukemia		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 7/11/2005 - Mar 2015	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 4/25/2006

**Study Objective:** To provide a classification guide that will organize the clinical and laboratory data necessary for assigning each patient with newly diagnosed ALL to a specific therapeutic trial. (2) To provide an administrative base to capture classification data for correlative studies accompanying current Children's Oncology Group (COG) ALL treatment protocols. (3) To provide a central reference guide for all required and research only studies that will be conducted at local and reference laboratories for all newly diagnosed patients with ALL. (4) To provide a mechanism for optional banking of leukemia and germ line specimens for current and future research.

**Technical Approach:** This COG risk group classification protocol will serve as a foundation for patients with newly diagnosed ALL. Registration on this protocol will be a requirement for entry onto any COG therapeutic study. The purpose of this classification protocol for ALL is to integrate data from recently completed clinical trials into an organized framework to appropriately risk stratify and treat patients enrolled in COG clinical trials for ALL. Patients will be assigned to an induction treatment regimen on the basis of studies that are performed at the host institution. Additional samples will also be sent by the local institution to one or more COG ALL reference labs at the time of diagnosis and at defined time points during therapy. This data will be used to refine subsequent therapy at the end of induction by assignment to a specific treatment protocol for defined risk groups in non-infant B-precursor ALL and/or via non-randomized allocation to specific treatment regimens within a given trial. The classification study will also be used for participation in companion biology research studies that are not used for treatment allocation and for voluntary banking of leukemia cells for future research. Approximately 8000 people will take part in this study across the United States and abroad. Madigan Army Medical Center plans to enroll 2-3 patients per year.

**Progress:** This protocol remains open to enrollment with three patients enrolled at MAMC, 2 during FY06. All three patients have been enrolled in treatment studies and are currently receiving treatment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205026	<b>Status:</b> Completed
<b>Title:</b> COG AAML03P1, Treatment of Newly Diagnosed Childhood Acute Myeloid Leukemia (AML) Using Intensive MRC-Based Therapy and Gemtuzumab Ozogamicin (GMTZ): A COG Pilot Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 3/16/2005 - Jan 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the safety of adding a single dose of gemtuzumab ozogamicin (GMTZ) to a well established intensive two-course MRC-based regimen (Medical Research Council) for remission Induction of children with newly diagnosed AML. (2) To determine the complete remission rate of a remission Induction regimen that consists of two consecutive courses of cytarabine, daunorubicin, and etoposide (ADE) plus a single dose of GMTZ in the initial course of ADE. (3) To determine the safety of adding a single dose of GMTZ to one course of post-remission Intensification therapy for children with newly diagnosed AML. (4) To determine the feasibility of performing biological studies (FLT3-ITD, MRD) for risk group stratification. (5) Feasibility component with the following objective: To determine the proportion of AML patients with primary induction failure (PIF) for whom a suitable unrelated stem cell donor can be made available within 21 days of study entry, and, identify obstacles to rapid donor identification..

**Technical Approach:** This study combines GMTZ with standard chemotherapy and consists of four phases. Patients with <20% blasts at the end of phase I (Induction I) receive phase II ADE. Patients in complete remission at the end of phase II (Induction II) proceed to phase III AE (Intensification #1). Patients with matched family donors who complete Intensification #1 and who remain in remission will be assigned to receive allogeneic BMT. Patients without matched family donors who complete Intensification #1 and who remain in remission will be assigned chemotherapy (MA+GMTZ followed by Capizzi II). This study will stop accruing when 150 patients have been evaluated. This accrual goal should be met in less than a year.

**Progress:** COG reported accrual goals reached as of 1 November 2005; no subjects enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205122	<b>Status:</b> Completed
<b>Title:</b> COG ACNS0126, A Phase II Study of Temozolomide in the Treatment of Children with High-grade Glioma or diffuse intrinsic Pontine Gliomas		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 8/22/2005 - Oct 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 7/18/2006

**Study Objective:** (1) To determine whether temozolomide given during radiation therapy and as adjuvant therapy results in an improvement in event-free survival compared to historical control cohorts. Target tumors are: Anaplastic Astrocytoma, Glioblastoma Multiforme, Gliosarcoma and Diffuse Intrinsic Pontine Gliomas. (2) To further assess the toxicity of temozolomide in a larger group of patients treated during XRT and during adjuvant treatment. (3) To evaluate the efficacy of temozolomide in the treatment of children with diffuse intrinsic Pontine gliomas. (4) To monitor the toxicity of this therapy in the treatment of children with diffuse intrinsic pontine gliomas. Laboratory Correlates (HGG Patients Only): (1) Investigate MGMT expression in formalin-fixed, paraffin-embedded biopsy specimens of brain tumors using immunohistochemical methods. (2) Identify those tumors in which MGMT expression is silenced by determining promoter CpG methylation in DNA isolated from formalin-fixed, paraffin-embedded tumor samples. (3) Investigate whether a functional MMR system is present in tumor cells by using microsatellite instability assays to compare DNA isolated from formalin-fixed paraffin-embedded tumor samples with DNA isolated from the patient's peripheral blood white cells. (4) Determine p53 expression using standardized immunohistochemical techniques. p53 mutation analysis will incorporate microdissection-based topographic genotyping and direct sequence analysis. (5) Determine MIB-1 indices in tumor samples using standardized immunohistochemical techniques.

**Technical Approach:** Temozolomide will be given concurrently with radiation therapy to newly diagnosed children with High Grade Glioma (HGG) or Diffuse Intrinsic Pontine Gliomas (DIPG) on a 42-day schedule. Four weeks following the completion of radiation therapy the patient will receive temozolomide daily for 5 days beginning a new cycle every 28 days for a total of 10 cycles. COG anticipates about 50 patients between the ages of 3 and 22 years of age will be participating in this study; enrollment at MAMC is estimated to be 1 to 2 patients per year.

**Progress:** This protocol closed to enrollment in July 2006. One MAMC subject enrolled but died of disease progression.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206034	<b>Status:</b> Ongoing
<b>Title:</b> COG ACNS0423: A Phase II Study of Concurrent Radiation and Temozolomide Followed by Temozolomide and Lomustine (CCNU) in the Treatment of Children with High Grade Glioma		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; LTC John B. Halligan, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 12/21/2005 - Mar 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 11/30/2006

**Study Objective:** (1) To determine whether temozolomide given during radiation therapy followed by the combination of Temozolomide and CCNU as adjuvant therapy results in an improvement in event-free survival compared to historical control cohorts. Target tumors are: o Anaplastic Astrocytoma; Glioblastoma Multiforme; Gliosarcoma. (2) To further assess the toxicity of adjuvant treatment with CCNU and temozolomide following XRT and concurrent temozolomide in a larger group of patients.

Laboratory Correlates: (1) Investigate MGMT expression in formalin-fixed, paraffin-embedded biopsy specimens of brain tumors using immunohistochemical methods. (2) Identify those tumors in which MGMT expression is silenced by determining promoter CpG methylation in DNA isolated from formalin-fixed, paraffin-embedded tumor samples. (3) Investigate whether a functional MMR system is present in tumor cells by using microsatellite instability assays to compare DNA isolated from formalin-fixed paraffin-embedded tumor samples with DNA isolated from the patient's peripheral blood white cells. (4) Determine p53 expression using standardized immunohistochemical techniques. p53 mutation analysis will incorporate microdissection-based topographic genotyping and direct sequence analysis. (5) Determine MIB-1 indices in tumor samples using standardized immunohistochemical techniques. (6) Determine the frequencies of GSTM1, GSTT1, and GSTP1 allelic variants in patients with high grade glioma. (7) Determine the level of protein expression of GSTP1 in tumor specimens. (8) Determine whether polymorphisms in GSTP1, GSTM1 and GSTT1 genes and tumor GSTP1 protein expression are associated with survival, hypothesizing that patients with inherent low activity GST genotypes and low GSTP1 protein expression will have increased survival time. (9) Assess whether germline polymorphisms of the GST genes are correlated with severity of chemotherapy toxicity, hypothesizing that patients with low activity GST genotypes will have decreased clearance of the metabolites of chemotherapy agents, and thus will have higher degree of toxicity. (10) Characterize allelic imbalance and copy number changes associated with high-grade gliomas by Affymetrix SNP arrays. (11) Characterize gene expression changes associated with high-grade gliomas by Affymetrix U133plus2 arrays. (12) To correlate any identified chromosomal abnormalities and differentially expressed genes with clinical parameters such as age, tumor location, degree of resection, histological grade, p53 expression, progression free survival, overall survival, treatment responses to determine their prognostic significance. (13) Identify oncogenes and tumor suppressor genes involved in the pathogenesis and malignant phenotype of pediatric high grade gliomas.

**Technical Approach:** Patients will be given radiation therapy (RT) to the brain 5 days a week for 6 weeks. Within the first week of starting RT the patient will begin taking Temozolomide orally (90 mg/m<sup>2</sup>/day) and continue taking the drug for 42 days (6 weeks). After completion of RT and the 6-week treatment with Temozolomide, patients will be given no treatment for a 4-week rest period. During Maintenance, patients will take oral Temozolomide again, but this time at a higher dose (160 mg/m<sup>2</sup>/day) for five days in a row followed by a 37 day break. In addition, patients will take another chemotherapy drug known as Lomustine (CCNU) orally with the temozolomide on day 1.

Patients will be treated on this study for about 11-12 months. Expected enrollment for MAMC is 1-2 patients per year.

**Progress:** This protocol remains open to patient entry, no patients have enrolled.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205084	<b>Status:</b> Ongoing
<b>Title:</b> COG AGCT0132, A Phase III Study of Reduced Therapy in the Treatment of Children with Low and Intermediate Risk Extracranial Germ Cell Tumors		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 11/25/2005 - Nov 2009	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 5/22/2006

**Study Objective:** Low Risk (LR) (1) To assess whether the proposed therapeutic plan can maintain a 3-year survival of at least 95% for patients newly diagnosed with Stage I gonadal malignant germ cell tumors. (2) To determine the cytogenetic and molecular genetic features which correlate with clinical differences in behavior. These tissues will be banked for future analyses of the biologic characteristics of malignant germ cell tumors.

Intermediate Risk (IR) (1) To assess whether three cycles of 3-day compressed PEB chemotherapy can maintain a 3-year event-free survival of at least 92% for patients with newly diagnosed Stage II-IV malignant testicular and Stage II-III ovarian germ cell tumors, newly diagnosed Stage I-II non-gonadal extracranial malignant germ cell tumors, or relapsed/progressed immature teratomas. (2) To determine the cytogenetic and molecular genetic features which correlate with clinical differences in behavior. These tissues will be banked for future analyses of the biologic characteristics of malignant germ cell tumors. (3) To assess whether three cycles of 3-day compressed PEB chemotherapy can maintain a 3-year survival of at least 95% for patients with newly diagnosed Stage II-IV malignant testicular and Stage II-III ovarian germ cell tumors, newly diagnosed Stage I-II non-gonadal extracranial malignant germ cell tumors, or relapsed/progressed immature teratomas with malignant components.

Cancer Control Objectives (1) To estimate the percentage of patients with Stage I ovarian and Stage I testicular GCTs for whom chemotherapy can be eliminated in the first three years following diagnosis. (2) To estimate the percentage of intermediate risk patients requiring only three cycles of therapy. (3) To delineate the acute toxicities and long term sequelae associated with therapy compression. These will be compared with historical data available from CCG-8882/POG-9049. (4) To determine the number of hospital days and total drug dosages required for the compressed therapy. These will be compared with historical data available from CCG-8882/POG-9049. (5) To compare the number of protocol directed treatment days of CCG-8882 with the number of treatment days used in AGCT0132.

Tumor Biology Objectives (1) To collect samples and facilitate studies of germ cell tumor cytogenetics and molecular genetics including deletion, mutation and imprinting on chromosomes 1 and 6, and amplification of c-myc. (2) To derive tumor cell lines and xenografts of germ cell tumors for use in studies of biologic agents and differentiation agents. (3) To establish a biologic samples bank for germ cell tumors to include frozen tumor and frozen normal tissue that may be used in future studies.

**Technical Approach:** AGCT0132 is a Phase III Study of Reduced Therapy in the Treatment of Children with Low and Intermediate Risk Extracranial Germ Cell Tumors. This study would avoid chemotherapy in low risk testicular/ovarian germ cell tumors by using surgery and observation. If during observation the tumor markers do not return to normal or become abnormal, the patient will be treated with chemotherapy in 3 cycles over a period of 9 weeks. Each treatment will involve 3 anti-cancer drugs: cisplatin, etoposide, and bleomycin. In patients with intermediate risk the

standard therapy would be surgery plus chemotherapy. The purpose of this study would be to decrease the total amount of chemotherapy given from 4 cycles to 3. The number of days chemotherapy would be given would also decrease from 5 to 3 days in each treatment cycle.

**Progress:** This protocol remains open to enrollment, with no patients enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203024	<b>Status:</b> Ongoing
<b>Title:</b> COG AHOD0031, A Phase III Group-wide Study of Dose-intensive Response-based Chemotherapy and Radiation Therapy for Children and Adolescents with Newly Diagnosed Intermediate Risk Hodgkin Disease		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 1/13/2003 - Mar 2008	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 12/12/2006

**Study Objective:** (1) To compare response-based therapy to standard therapy for intermediate risk Hodgkin disease. (2) To determine whether involved field radiation therapy (IFRT) can be eliminated based upon early and complete response to multiagent chemotherapy. (3) To determine whether the addition of an additional two cycles of chemotherapy (DECA) can improve outcome in those with a slow early response to standard chemotherapy. (4) To prospectively collect information on the individual prognostic significance of the following presenting factors: erythrocyte sedimentation rate, circulating levels of IL-100, each of the "B" symptoms - fever, night sweats, weight loss, nodal aggregate > 6cm, large mediastinal mass > 1/3 thoracic diameter and number of involved nodal sites, histology, albumin, blood counts, sex and age. (5) To study the reliability and utility of [18F] - Fluorodeoxyglucose (FDG) Imaging (PET scans) as an imaging modality in Hodgkin disease. (6) To determine the frequency and severity of late effects of therapy including thyroid dysfunction, infertility, cardiotoxicity, pulmonary toxicity and second malignant neoplasms. (7) To serve as the therapeutic companion to biology and late effects studies in Hodgkin disease and correlate those results with response to therapy, event free-survival and overall survival.

**Technical Approach:** All patients will receive 3 cycles of ABVE-PC three weeks apart followed by a re-evaluation of disease. Those with a rapid early response will receive an additional 1 cycle of ABVE-PC three weeks later followed by another re-evaluation of disease. Rapid early responders, who have sustained a complete response following a total of 4 cycles of ABVE-PC chemotherapy, will be randomized to omit (reduced therapy arm) or receive consolidative low dose involved field radiation therapy (IFRT) (standard therapy arm). Those with less than a complete response will receive IFRT. Patients with a slow early response to 3 cycles of ABVE-PC will be randomized to receive 1 additional cycle of ABVE-PC (standard therapy arm) alone versus 1 additional cycle of ABVE-PC preceded by 2 cycles of DECA (augmented therapy arm). All patients who are slow early responders will receive consolidative low dose IFRT. Patients with less than a complete response after consolidative radiation therapy or those with progressive disease at any time will be treated at the discretion of the treating physician after consultation with the study chair.

**Progress:** This protocol remains open to patient entry with two patients enrolled, none during FY06. One patient had recurrent disease and enrolled in another COG protocol. The other patient continued to be followed at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205047	<b>Status:</b> Completed
<b>Title:</b> COG AHOD00P1, A Pilot Study of Re-Induction Chemotherapy with Ifosfamide, and Vinorelbine (IV) in Children with Refractory/Relapsed Hodgkin Disease		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 5/31/2005 - Jan 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** (1) To determine the response rate of the re-induction regimen ifosfamide/vinorelbine (IV) with filgrastim overall and within the cohorts of minimally pre-treated/low risk and heavily pre-treated/high risk patients with relapsed/refractory Hodgkin disease. (2) To evaluate ifosfamide/vinorelbine (IV) with filgrastim as a re-induction regimen in minimally pretreated/low risk pediatric patients with relapsed/refractory Hodgkin disease. Specifically, to determine: (a) the cardiac, hepatic, renal, and hematologic toxicity, and toxic death rate and (b) the proportion of patients able to mobilize sufficient hematopoietic stem cells (CD34+) after 2 cycles of IV. To collect data regarding tumor biologic characteristics in patients with relapsed/refractory Hodgkin disease (a) To determine the incidence of hyper mutability in Hodgkin patients by longitudinal genotoxic bio-monitoring and (b) To determine the prognostic significance of biologic markers including serum IL-10 receptor, serum IL-2 receptor, p53, and mdm-2.

**Technical Approach:** This is a phase II pilot study of re-induction chemotherapy with Ifosfamide and Vinorelbine (IV) in children with refractory/relapsed Hodgkin disease. Subjects will have two cycles of chemotherapy, Ifosfamide and Vinorelbine, at least 21 days apart. Filgrastim will be given on day 6 of each cycle, or anytime tests show the white blood cell count is too low, to help white-blood cells grow. Subjects will be evaluated at the end of cycle 2. Subject's whose disease worsens will be taken off study therapy. Subject's whose disease remains the same will have a stem cell collection and then be taken off study therapy. Subject's whose disease responds to treatment will have a stem cell collection at the end of cycle two. Stem cell transplantation will not be performed at MAMC; subjects will be referred to a COG approved bone marrow transplant center.

**Progress:** COG closed enrollment in March 2006, with no subjects enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205014	<b>Status:</b> Ongoing
<b>Title:</b> COG AHOD0321, A Phase II Study of Weekly Gemcitabine and Vinorelbine in Children with Recurrent or Refractory Hodgkin Disease		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 12/6/2004 - Dec 2005	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 10/24/2006

**Study Objective:** To determine the response rate after weekly administration of the combination of gemcitabine and vinorelbine to patients with recurrent or refractory Hodgkin Disease. To document the toxicity of weekly administration of gemcitabine and vinorelbine in patients with recurrent or refractory Hodgkin Disease.

**Technical Approach:** This is a Phase II study of weekly Gemcitabine and Vinorelbine In children with recurrent or refractory Hodgkin Disease. This study will evaluate the use of a new re-induction chemotherapy regimen consisting of the anti-cancer drugs combination of gemcitabine and vinorelbine in patients who have previously been treated for Hodgkin Disease. Patients will receive at least two cycles (21 days each) of weekly GEM/VINO therapy. The goal is to determine if the combination of these is active against recurrent Hodgkin Disease and to find out what effects this drug combination will have. Patients with any response after the first two cycles may elect to proceed directly to stem cell transplantation. Those with stable disease after the first two cycles, will receive a minimum of two more cycles of GEM/VINO. At the end of the fourth cycle, patients without progressive disease can remain on study and continue to receive GEM/VINO or go off study for alternative therapy. About 26 patients between the ages of 0 to <30 years of age will be participating in this study.

**Progress:** This protocol remains open to enrollment with one patient enrolled who is off study treatment but continued to be followed at MAMC after having gone through bone marrow transplant.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201108	<b>Status:</b> Ongoing
<b>Title:</b> COG ANBL00B1, Neuroblastoma Biology Studies		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 6/26/2001 - May 2007	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** (1) To prospectively analyze the factors that are currently used for risk-group assignment (DNA content by flow cytometry, MYCN copy number by FISH, and tumor histology using the International Neuroblastoma Pathologic Classification System) in neuroblastoma tumors at the time of diagnosis, (2) to maintain a reference bank containing clinically and genetically characterized frozen tumor tissue, tumor DNA and RNA, tumor touch preparations, histology slides and blocks, cell lines, and paired normal DNA obtained at the time of diagnosis (all patients), at the time of second-look surgery (high-risk patients), and relapse (all patients) for future research studies, (3) to prospectively analyze the prevalence of 1p, 11q, 14q LOH and gain of 17q; the expression of nerve growth factor (NGF) and its high affinity (Trk-A) and low affinity (p75 NTR) receptors; and telomerase activity in diagnostic neuroblastoma tumors, and to determine the independent clinical significance of these biologic factors compared to MYCN amplification, INSS stage, age, and histologic variables in predicting either response to treatment or outcome, (4) to build a database of the known biologic prognostic factors for patients on therapeutic studies, (5) to serve as a Registry for neuroblastoma patients whose tumors demonstrate clinical and genetic features defined as "Low Risk" for treatment failure in the absence of adjuvant therapy, and (6) A secondary objective of this study is to prospectively analyze the role of ferritin, LDH, and Imaging-defined risk factors identified at the time of diagnosis in risk assessment.

**Technical Approach:** Clinical and biological factors have been shown to have prognostic value in neuroblastoma. Current therapeutic studies for neuroblastoma patients are tailored according to patient risk. In the Children's Oncology Group (COG), risk-group assignment is currently based on INSS stage, age, MYCN copy number, tumor cell ploidy, and Shimada tumor histopathology. However, additional factors have also been shown to have prognostic value including the level of Trk-A expression, multi-drug resistance associated protein (MRP) expression, telomerase activity, CD44 expression, and genetic abnormalities including LOH of 1p, 11q, 14q and gain of 17q. We hypothesize that analyzing additional genetic and biologic factors will result in a further refinement of the current COG risk-group schema, and will, thereby, impact future risk-based approaches to therapy. We further hypothesize that maintaining tumor and nucleic acid banks with well characterized samples will provide invaluable biologic resources for future research studies that will lead to a further understanding of neuroblastoma biology and the development of new, effective therapy for high-risk patients.

**Progress:** This study remains open to patient entry, with three patients enrolled at MAMC, two during FY06. One patient was transferred to Seattle Children's Hospital in July 2006. Data on the two remaining patients continued to be submitted to COG.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205069	<b>Status:</b> Completed
<b>Title:</b> COG ANHL0121, A Phase II Study of Rituximab (IND#7028) and Ifosfamide, Carboplatin and Etoposide (ICE) Chemotherapy in Children with Recurrent/Refractory B-cell (CD20+) Non-Hodgkin Lymphoma and B-cell Acute Lymphoblastic Leukemia		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 7/6/2005 - Nov 2007	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** Primary Aims: (1) To determine the response and relapse-free survival rates to chemotherapy with ifosfamide, Carboplatin, and etoposide plus rituximab for patients with recurrent/refractory CD 20+ NHL and B-cell ALL. (2) To evaluate the toxicity profile of this therapy regimen. Specifically, the frequency of therapy delays between courses due to prolonged Grade 4 hematologic toxicity will be monitored. Secondary Aims: (1) To determine whether ifosfamide, Carboplatin, and etoposide in combination with rituximab and G-CSF will result in mobilization of greater than  $2 \times 10^6/\text{kg}$  peripheral blood stem cells (CD34+ cells, PBSC) in at least 80% of patients for whom peripheral stem cell collection is performed. (2) To evaluate the time course of engraftment for patients who undergo peripheral stem cell transplantation following collection of stem cells using this mobilization regimen. (3) To collect tumor specimens to permit an evaluation of gene expression profiles in patients with recurrent/refractory CD20+ NHL and B-cell ALL. (4) To collect tumor and other specimens to permit the identification of patient-specific markers for use in evaluation of presence and significance of minimal residual disease.

**Technical Approach:** This study will address adding an investigational drug, Rituximab, to standard chemotherapy called ICE (ifosfamide, Carboplatin, and etoposide) in an attempt to improve the outcome of patients who have not responded well to standard treatment alone. Patients will be on this study for up to three months, depending on how the disease is responding to treatment. Patients who have disease which gets worse after one course of chemotherapy will not continue on the study drugs. Patients who have disease that stays the same or responds at all to treatment will receive a second course of therapy. There will be a third course of therapy for patients who show a continued response. Some patients may have peripheral blood stem cells collected during therapy which would be stored and used later in case patients need more treatment.

**Progress:** This protocol closed to accrual on 23 Oct 2006, with no MAMC subjects enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200049	<b>Status:</b> Ongoing
<b>Title:</b> COG D9902, A COG Soft Tissue Sarcoma Diagnosis, Biology and Banking Protocol		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 2/22/2000 - Feb 2010	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 1/19/2006

**Study Objective:** (1) To facilitate the collection of human tissue and other biologic specimens (blood, bone marrow) from Intergroup Rhabdomyosarcoma Study Group (IRSG) investigators, (2) To provide a repository for long-term storage of tissue and other biologic specimens (blood, bone marrow) collected by IRSG investigators (referred to as the Bank), and (3) To make available, through the IRSG/Cooperative Human Tissue Network, these materials for approved projects by laboratory-based investigators.

**Technical Approach:** At the time of initial diagnosis of rhabdomyosarcoma or undifferentiated sarcoma (or at re-excision of the primary tumor, if it occurs prior to the start of chemotherapy), surgical tissue, bone marrow and blood that are no longer needed for diagnosis will be prepared and shipped to the Pediatric Cooperative Human Tissue Network (CHTN) for Banking and Distribution.

**Progress:** This protocol is open to patient entry with two patients enrolled at MAMC, none during FY06. Both patients have moved out of the MAMC area. Follow up data is not required under this tissue banking protocol.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 98090	<b>Status:</b> Ongoing
<b>Title:</b> COG P9442: National Wilms Tumor Late Effects Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 7/17/1998 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 6/20/2006

**Study Objective:** To determine (1) the frequency of Wilms tumor and other cancers in family members of Wilms tumor patients in order to estimate the recurrence risk in siblings and offspring; test the plausibility of specific genetic modes of inheritance in homogeneous subgroups; and identify familial cancer syndromes (if any) that may involve Wilms tumor, (2) To determine fertility rates of Wilms tumor patients and rates of perinatal mortality, low birth-weight and adverse pregnancy outcomes in relation to the type and amount of cancer treatment received in childhood, (3) To estimate the rates of selected congenital defects and of specified single gene disorders (sentinel phenotypes) in the offspring of Wilms tumor patients, (4) to estimate the rates of second malignancy neoplasms in relation to the dosage of radiation therapy and the use of specific chemotherapeutic agents (Actinomycin D, doxorubicin, Cytosan and etoposide) received in childhood, (5) to compare the incidence rate of congestive heart failure among Wilms tumor survivors in relation to the dose of radiation therapy received to abdomen and/or lungs and to the use of specific chemotherapeutic agents.

**Technical Approach:** The large number of Wilms tumor survivors ascertained by the NWTs during its first twenty years of operation constitutes an ideal cohort for the study of familial risk and late effects of treatment. Four protocol studies have been conducted; treatment protocols and results for the first three studies have been published. A large fraction of the total national U.S. incidence of Wilms tumor has been registered on these studies, probably as much as 70% of an estimated 450-500 cases occurring nationally since 1980. Over 2,500 children who were followed on NWTs treatment protocols have now survived 5 or more years since their original diagnosis. Many of those treated more than a decade ago have reached sexual maturity, so that their reproductive history and the status of their offspring may be evaluated by entry into this study.

**Progress:** This protocol remains open to enrollment with no subjects enrolled to date at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201054	<b>Status:</b> Completed
<b>Title:</b> COG P9934: Systemic Chemotherapy, Second Look Surgery and Conformal Radiation Therapy Limited to the Posterior Fossa and Primary Site for Children > 8 Months and < 3 Years with Non-metastatic Medulloblastoma - A Children's Oncology Group Phase III Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; COL John D. Werschkul, MC; COL Marc G. Cote, MC; LTC William B. Reece, MC		
<b>Start - Completion:</b> 1/23/2001 - Jan 2006	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 1/4/2006
<b>Study Objective:</b> (1) To determine if the proposed treatment for children > 8.0 months and < 3 years of age at registration with non-metastatic (M0) medulloblastoma is more effective than the combined treatments given to children of the same age and extent of disease on POG 9233, as measured by event-free survival (EFS) rates, (2) to assess the feasibility and safety of the planned use of second look surgery and focal conformal radiation therapy following chemotherapy, (3) to determine the acute and chronic toxicities associated with the above treatment regimens, (4) to describe the neuropsychological and neuroendocrine effects of this systemic chemotherapy, surgery, and local, conformal radiation, (5) to determine the feasibility and validity of a centralized telephone interview based data collection method for neuropsychological evaluations, and (6) to determine the incidence of atypical teratoid/rhabdoid tumor (AT/RT) in children enrolled on this study.		
<b>Technical Approach:</b> In this study for young children with relatively low risk medulloblastoma, we will test a new therapeutic approach which begins with maximal safe tumor resection and a 16-week, 4-drug induction chemotherapy regimen of cyclophosphamide, vincristine, cisplatin, and oral etoposide. In comparison to the chemotherapy regimens of studies 8633 and 9233, cisplatin is introduced earlier, and given concurrently with the other agents. As well, etoposide is given in an oral form. Based upon the compelling data that outcome is clearly linked to a complete surgical resection the proposed therapy includes a 'second look' surgery following induction chemotherapy in an attempt to resect residual disease in those patients who have failed to achieve a complete response to chemotherapy. To improve local control rates this clinical trial will test the use of conformal radiation therapy and will determine if these techniques can reduce radiation-related side effects. Following recovery from the initial phase of treatment, patients will receive a maintenance phase of chemotherapy, using cyclophosphamide, vincristine, and the prolonged administration of oral etoposide, to complete one year of therapy.		
<b>Progress:</b> This protocol closed enrollment in June 2006, with no subjects enrolled at MAMC.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205105	<b>Status:</b> Ongoing
<b>Title:</b> COG-LTF, A Groupwide Process for Collecting Long Term Follow Up Data		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC; MAJ Melissa A. Forouhar, MC		
<b>Start - Completion:</b> 7/12/2005 - indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 6/20/2006

**Study Objective:** The specific objective is to establish a single mechanism for regular annual local Institutional Review Board (IRB) approval for COG member institutions by aggregating protocols for which only follow-up data collection is needed.

**Technical Approach:** This document is designed to facilitate follow-up data collection for Children's Oncology Group (COG) studies that are closed to accrual and for which all patients in an institution have completed therapy. This includes studies that originated in the Children's Cancer Group (CCG), the Pediatric Oncology Group (POG), the Intergroup Rhabdomyosarcoma Study Group (IRSG), and the National Wilms Tumor Study Group (NWTSG) as well as new COG studies.

**Progress:** This protocol remains ongoing with 31 patients now being followed under this long-term administrative protocol. No patients were entered during. Twenty nine continued to be followed; two are not lost to follow up.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 94092	<b>Status:</b> Ongoing
<b>Title:</b> POG 9351/CCG 7921: Trial of Doxorubicin, Cisplatin, and Methotrexate With and Without Ifosfamide, With and Without Muramyl Tripeptide Phosphatidyl Ethanolamine (MTP-PE) for Treatment of Osteogenic Sarcoma		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieu, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 4/21/1995 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 3/21/2006

**Study Objective:** (1) To improve the survival of patients with osteogenic sarcoma, (2) To compare the results of a prospective, randomized trial of two chemotherapeutic regimens in the treatment of osteogenic sarcoma, (3) To compare the results of a combined chemotherapeutic regimen (high-dose methotrexate, cisplatin, and doxorubicin) given pre-operatively and post-operatively to a similar regimen using the same drugs and adding ifosfamide, (4) To test whether the early introduction of ifosfamide results in a higher rate of good histologic response at the time of definitive surgery, (5) To determine whether histologic response assessed after longer pre-operative chemotherapy with more drugs predicts disease-free survival with the same power as observed in CCG-782 which used a shorter period of pre-operative chemotherapy and fewer drugs, (6) To determine whether liposomal muramyl tripeptide-phosphatidyl ethanolamine (MTP-PE, CGP 19835a), a stimulator of macrophage function, can improve disease-free survival for patients with osteogenic sarcoma, (7) To determine whether multiple drug resistance gene-encoded P-glycoprotein expression is useful for determine prognosis or assigning therapy.

**Technical Approach:** This study is a phase III, prospective, randomized trial of two chemotherapy regimens for the treatment of newly diagnosed, previously untreated osteogenic sarcoma. One regimen calls for the administration of high-dose methotrexate, doxorubicin, and cisplatin. The other regimen calls for the administration of these agents plus ifosfamide. Chemotherapy is administered for 10 weeks prior to surgical resection of the primary tumor and any metastatic disease (CCG patients). Patients also are randomly assigned either to receive muramyl tripeptide (MTP-PE) with maintenance chemotherapy or to receive maintenance chemotherapy alone.

**Progress:** This protocol closed to patient entry November 1997, with two patients enrolled. One patient chose to discontinue treatment and the other patient completed study therapy. Long-term follow-up data continues to be submitted annually to COG on both patients.

A final report on this protocol was submitted by the study chair, Paul Meyers, M.D., 26 October 2004. Summary of recommendations and future plans: Regimen A, which calls for cisplatin, doxorubicin, and high dose methotrexate, achieved EFS at least as good as regimen B, which calls for the same three agents with the addition of ifosfamide. Regimen A had less toxicity than regimen B. Until an appropriate prospective randomized trial is available, regimen A should be considered standard therapy for osteosarcoma. The interaction between MTP and ifosfamide needs further study. In vitro analysis of the interaction should be encouraged and clinical trials considered of the combination in patients at the time of recurrence.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 95058	<b>Status:</b> Completed
<b>Title:</b> POG 9400: ALinC 16 Classification (C) Protocol		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 12/16/1994 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 11/15/2005

**Study Objective:** (1) To continue to characterize the biologic findings of the acute lymphoblastic and undifferentiated leukemias (immunologic markers, ploidy (DNA index), karyotyping, morphology) and their relationship, as prognostic factors for attaining and maintaining remission, (2) To apply to therapy selection, the determination that ploidy and certain structural chromosomal abnormalities predict poor prognosis, (3) To evaluate the usefulness of PCR technique in detecting minimal residual disease in patients with disease demonstrating t ( 9; 2 2 ) or t ( 1; 19 ) chromosomal abnormalities. (optional), (4) To apply to therapy selection molecular testing for 11q23 translocation in infants < 12 months of age with acute lymphocytic leukemia, (5) To determine the roll of p53 and pl6 tumor suppressor genes in T-ALL. (optional), (6) Individual patient outcome will be compared with the leukemia cell proliferation response to ask if proliferation in response to a myeloid growth factor is associated with an increased risk of developing AML. (optional), (7) To determine risk group assessment using Fluorescent In-Situ Hybridization (FISH) screening for Trisomies 4 and 10 in Non-T, Non B ALL, and (8) To determine if drug sensitivity profiles of blast cells for three commonly used chemotherapeutic agents - Adriamycin, Methotrexate, and Cytarabine correlate with a) initial response b) subsequent development of relapse.

**Technical Approach:** A bone marrow aspirate (a needle stick in hip bone to draw marrow into syringe) will be done to prove or disprove diagnosis of leukemia. If leukemia is present, it is important to identity the exact type and subtype of leukemia, in order to plan treatment. This typing requires that several laboratory tests be run on the leukemia cells in the bone marrow. As we perform the bone marrow aspiration we will be removing enough bone marrow (about 2-1/2 teaspoons) to run the laboratory tests. We may also need to draw some blood (about 2-1/2 teaspoons) from a vein to send for studies. Some of these tests will be done here and some will be sent to reference laboratories in other Pediatric Oncology Group institutions for different kinds of special tests to identify the characteristics of the leukemia cells.

**Progress:** This protocol closed to patient entry in November 1999, with nine patients enrolled. One patient has been reported lost to follow up, one patient transferred to another COG institution, one patient relapsed, and six patients continue to be followed. COG reported the protocol completed 31 March 2000, with a final accrual of 4211 (842 per year). Hard copy of the final report has been placed in the protocol file.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 96097	<b>Status:</b> Ongoing
<b>Title:</b> POG 9440: National Wilms Tumor Study - 5: Therapeutic Trial and Biology Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 4/19/1996 - Indef	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 3/21/2006

**Study Objective:** (1) To increase the survival rate of children with favorable histology Wilms tumor and other renal tumors of childhood, (2) to determine if loss of heterozygosity for chromosome 16q markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (3) to determine if loss of heterozygosity for chromosome 1p markers in tumor tissue is associated with a poorer prognosis for children with favorable histology Wilms tumor, (4) to determine if increased DNA content in tumor cells is associated with a poorer prognosis, (5) to decrease the acute and long term morbidity of treatment of children with Wilms tumor, (6) to improve the survival of patients with unfavorable histology tumors including Wilms tumor with diffuse anaplasia and clear cell sarcoma of the kidney by using a new treatment regimen that includes etoposide and cyclophosphamide, (7) to improve survival of patients with malignant rhabdoid tumor of the kidney, (8) to study biology and pathology of patients who present with bilateral Wilms tumor, (9) to conduct hypothesis-driven trials led by diagnostic radiologists in order to develop guidelines, and (10) to establish a biological samples bank containing touch preparations, paraffin blocks, frozen tumor, normal kidney tissue, and serum and urine.

**Technical Approach:** This proposed therapeutic trial involves a number of experimental regimens that are designed either to reduce treatment for the subgroup of patients with the most favorable prognosis, or to intensify treatment for several subgroups with the least favorable prognosis. Patients will be stratified into the appropriate treatment regimens by age, size of tumor at diagnosis and staging of the tumor (Stages 1-V) with favorable/unfavorable histology, including rhabdoid, clear cell sarcomas and Wilms tumor with diffuse or focal anaplasia. Treatment will include nephrectomy or surgical debulking of tumor, radiation therapy to abdomen and/or lungs, and appropriate chemotherapy regimens.

**Progress:** This protocol closed to patient entry in June 2002, with two patients enrolled who continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200018	<b>Status:</b> Completed
<b>Title:</b> POG P9761: Phase II Trial of Irinotecan in Children with Refractory Solid Tumors: A COG Study		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 11/19/1999 - Nov 2004	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 10/14/2005

**Study Objective:** (1) To determine the efficacy of Irinotecan in the treatment of children with refractory neuroblastoma, sarcomas of soft tissue or bone, other solid tumors, or brain tumors, (2) to further evaluate the toxicity of Irinotecan when given daily for 5 days, repeated every 21 days, and (3) to further evaluate the pharmacokinetics/pharmacodynamics of Irinotecan and its metabolites SN-38, SN 38G, and APC, using a limited sampling strategy.

**Technical Approach:** Irinotecan appears to be one of the most active topoisomerase I inhibitors that is clinically available and therefore deserves further evaluation in children with recurrent CNS or solid tumors. Although the optimal schedule for Irinotecan is not yet known, antitumor activity has been observed on all schedules of administration. Pharmacokinetic studies, an integral component of this trial will be done to determine if there are correlates with PK parameters and toxicity or response.

**Progress:** This protocol reached its accrual goals and was reported completed in November 2005. One patient had been enrolled at MAMC during FY00, but died due to progressive disease.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200048	<b>Status:</b> Ongoing
<b>Title:</b> POG P9851: Osteosarcoma Biology Protocol, Companion to Group-Wide Therapeutic Studies		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 2/22/2000 - Feb 2010	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 1/18/2006

**Study Objective:** (1) To increase our understanding of the basic biology of these tumors, with a distinct possibility that new therapeutic targets may be uncovered. Examples of this type are ErbB-2 and methotrexate resistance factors, (2) To develop a set of biologic prognostic indicators which can be measured at diagnosis and which will be predictive of response and outcome in osteosarcoma. These could then be used in subsequent treatment programs to determine therapy, avoiding excessive toxicity to good risk patients and reserving alternative, more intensive therapy for those at standard risk. Examples include loss of heterozygosity at Rb and MDR, (3) To determine the feasibility of various assays and to develop a reliable mechanism of distributing osteosarcoma samples to various intergroup investigators, with centralized reporting of laboratory results and adequate quality control.

**Technical Approach:** At the time of biopsy or surgery (definitive or recurrence), tumor tissue that is not needed for diagnosis will be processed and forwarded to the Cooperative Human Tissue Network (CHTN) for distribution. Specimens will include: tumor tissue (Formalin-fixed or formalin-fixed paraffin embedded block or 30 unstained slides; blood samples (heparinized (10 ml), serum (14 ml)). Assays being performed: MDR Immunohistochemistry (University of Rochester); MDR Functional Assays/MRP (Memorial Sloan-Kettering); Methotrexate Transport & Metab (Memorial Sloan-Kettering); Topoisomerase II (Yale University); Bcl-2/Bax (Yale University); Rb/p53 (Fels Institute); ErbB-2 (Memorial Sloan-Kettering); MDM2 (Memorial Sloan-Kettering); p16/p21 (Hospital for Sick Children); LOH at 3q,18q (Fels Institute); sis,gli,fos (Yale University); SV40 (University of Colorado); myc,RAS (Memorial Sloan-Kettering); metalloproteinase (Yale University); c-met/HGF (Yale University); IGF-I/IGF-IR (University of Maryland); Telomerase (St. Jude Children's); Ploidy (Dana Farber).

**Progress:** In July 2006, COG reported that this companion protocol would be phased out and expected to close accrual within six months after the new protocol is up and running. One patient was enrolled at MAMC and continues to be followed, pending close-out of this protocol by COG.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203105	<b>Status:</b> Completed
<b>Title:</b> POG P9962 A Phase II Study of Intrathecal Topotecan in Patients with Refractory Meningeal Malignancies		
<b>Principal Investigator:</b> MAJ Kenneth H. Lieuw, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kelly J. Faucette, MC		
<b>Start - Completion:</b> 11/17/2003 - Aug 2008	<b>Funding:</b> COG/POG via The Geneva Foundation	<b>Periodic Review:</b> 7/27/2005

**Study Objective:** (1) To determine the therapeutic activity (response rate and time to CNS progression of intrathecal Topotecan in patients with recurrent or refractory neoplastic meningitis. (2) To further assess the safety/toxicity of intrathecal Topotecan in the treatment of patients with neoplastic meningitis. (3) To evaluate the concentration of matrix metalloproteinases (MMPs) in the CSF of patients with recurrent or refractory neoplastic meningitis.

**Technical Approach:** A Phase II study for children and adolescents, 1 - 21 years of age with neoplastic meningitis using Topotecan administered directly into the cerebrospinal fluid to stabilize or shrink the cancer and give relief of cancer symptoms.

**Progress:** COG permanently closed this protocol 7 April 2006, due to low accrual. No patients enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206045	<b>Status:</b> Completed
<b>Title:</b> The Pontine Valentine Leucocidin Virulence Factor in Staph Aureus Disease: A Retrospective Study Analyzing CA-MRSA Incidence and Clinical Severity		
<b>Principal Investigator:</b> CPT Ashley M. Maranich, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Mary P. Fairchok, MC; MAJ Steven D. Mahlen, MS		
<b>Start - Completion:</b> 1/19/2006 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objectives are to determine the proportion of Panton-Valentin leukocidin (PVL) positive strains of Staphylococcus aureus isolated in the MAMC Clinical Microbiology Lab and to determine if PVL positivity is correlated with CA-MRSA strains. Secondary objectives are to compare the clinical course of infections with PVL positive strains and PVL negative strains through chart review.

**Technical Approach:** 538 clinical isolates of S. aureus have been tested by the MAMC clinical microbiology lab for PVL toxin positivity by real-time PCR. This study proposes to access these results and exclude duplicate isolates from the same infection as well as isolates that were obtained for surveillance purposes only, then determine the proportion of isolates that were PVL positive and separately analyze the proportion that were PVL positive for CA-MRSA versus nosocomial MRSA and MSSA strains. Antibiotic susceptibility (to include D-test status for erythromycin inducible clindamycin resistance) will be accessed to categorize the strains as MSSA, nosocomial MRSA and CA-MRSA.

Outpatient and inpatient charts will be assessed from patients corresponding to the S. aureus isolates and reviewed for the following clinical parameters: severity of infection, type of infection, need for hospitalization, antibiotic regimen prescribed, route of antibiotic administration (IV vs. PO vs. both), necessity for incision and drainage, number of clinic and/or ED visits related to infection, recurrence of disease, prescription of eradication regimen.

**Progress:** This protocol was reported completed in June 2006. Results: Complete data was available for 331 of 407 samples (82%). MRSA was more likely to be PVL+ than MSSA (166/201; 81% versus 31/130; 24%),  $p=.001$ . Disease characteristics associated with all PVL- strains were the same as the MRSA PVL+ subset, with the exception that there was no increased need for I&D in the MRSA PVL+ versus PVL- strains. Although PVL+ strains were less likely to require hospitalization, they were associated with more outpatient visits than PVL- strains (3.56 versus 2.55,  $p<.02$ ).

**Conclusion:** PVL is more likely to be associated with methicillin-resistance and community-acquired SA infections. However, the study found that PVL+ strains were less likely to cause invasive disease needing IV antibiotics or hospitalization. Controlling for MRSA+, PVL+ strains were also no more likely to require I&D than PVL- strains. However, PVL does seem to cause a higher healthcare burden with more recurrence and an increased number of outpatient visits.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204040	<b>Status:</b> Ongoing
<b>Title:</b> National Cystic Fibrosis Foundation Patient Data Registry		
<b>Principal Investigator:</b> COL (Ret) Donald R. Moffitt, MD		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Dana A. Winter, C.R.T.		
<b>Start - Completion:</b> 2/6/2004 - Indef	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/13/2006

**Study Objective:** (1) Monitoring epidemiologic trends in the population for CF patients in the US through data collection and entry into the NCF Foundation Patient Registry. (2) Assist in development of therapeutic advances responsible for the improved survival of cystic fibrosis patients.

**Technical Approach:** The CF Patient Data Registry will include patients with cystic fibrosis who are cared for at CF Care Centers throughout the U.S. Locally, this project will include patients from the CF Care Center at Madigan Army Medical Center, which currently cares for 27 CF patients. When a patient and/or parent gives written consent to be included in the registry, updates of the patient's medical information will be sent to the CF National Patient Registry. The information that is sent to the National Patient Registry includes patient name, date of birth, social security number, and zip code of residence. Personal identifiers allow the CF National Patient Registry to track information for patients who receive care at more than one CF center or who move between CF centers. Patients have the choice of participating in the registry without sending the patient's social security number to the CF National Patient Registry. Other information that is sent to the CF National Patient Registry includes the following: specifics of diagnosis (e.g., diagnosis date, sweat test results, genotype); clinical status (e.g., presence of complications, transplant status); test results (e.g., pulmonary function tests, microbiology cultures); nutritional status (e.g., height, weight, nutritional supplements, pancreatic enzyme use); treatment information (e.g., hospitalizations, home therapies, use of new therapies ); participation in clinical trials; and demographic data (e.g., educational status, marital status, employment status, and insurance coverage).

**Progress:** This database protocol remains open to enrollment, with 18 patients enrolled MAMC, none during FY06. Patient data continues to be collected and submitted to the Cystic Fibrosis Foundation on MAMC patients enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204028	<b>Status:</b> Ongoing
<b>Title:</b> Pediatric Intubation Training Utilizing the Ferret (mustela putorius furo) Model		
<b>Principal Investigator:</b> LTC Robert A. Puntel, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Catherine Kimball-Eayrs, MC		
<b>Start - Completion:</b> 12/17/2003 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11/8/2006

**Study Objective:** This is a training protocol using a ferret model to teach physicians and other health care professions how to endotracheally intubate (i.e. place a plastic tube in the windpipe) neonates and infants. The training is part of a two-day course in pediatric life-saving techniques; the class is called Pediatric Advanced Life Support (PALS) and is developed by the American Heart Association. PALS is offered through the Department of Emergency Medicine two to four times a year.

**Technical Approach:** Students will complete classroom instruction in principles and techniques of pediatric life support. The students will then practice techniques, include endotracheal intubation, on mannequins. Following this practice, students will intubate an anesthetized ferret, which more closely simulates the respiratory anatomy and reflexes of a human child than does a mannequin. Up to six ferrets will be used for each training session and each ferret will serve to train four physicians or other health care providers. The ferrets will be fully anesthetized and will experience no pain during the procedure; they will be closely monitored and observed by a member of the veterinary staff. During the procedure, each of the course participants will learn to place a small plastic tube through the mouth and into the trachea (windpipe) of an anesthetized ferret with the assistance of a small, lighted metal blade called a laryngoscope. The investigators, other course instructors, and veterinary staff will directly supervise the procedure. If any ferret is traumatized or shows signs of problems with the anesthetic drugs, the procedure will be stopped on that animal. No animal will undergo more than seven intubation attempts. After the training session is complete, the animals will be allowed to wake up from anesthesia and will be returned to their usual housing at the MAMC Animal Facility. In the first days following the procedure, the ferrets may experience a mild sore throat, and they will be offered moist food as needed. Ferrets will be housed and maintained according to standard animal husbandry protocols.

**Progress:** Four PALS courses were held in FY 2006 with 88 medical personnel successfully trained using many simulators and 10 ferrets for tracheal intubation training. With the new SimBaby model, ferret use is less than in previous years. Expect to eventually phase out use of live animals due to the quality of simulation trainers becoming available. Four labs are planned for FY 2007.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203046	<b>Status:</b> Ongoing
<b>Title:</b> Telemedicine Based Ultrasound for Detecting Neonatal Heart Disease in Babies at Remote Military or Native American Health Care Facilities		
<b>Principal Investigator:</b> LTC Robert A. Puntel, MC		
<b>Department:</b> Pediatrics	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL James B. Kinney, MC; COL David T. Estroff, MC; David J. Sahn, MD; COL (Ret) Edward R. Carter, MD; Mark D. Reller, MD		
<b>Start - Completion:</b> 7/22/2003 - Dec 2006	<b>Funding:</b> DCI via Grant	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** This impact and outcomes research proposal will specifically test the hypothesis that a method for reliable and rapid assessment of newborn infants at risk for heart disease can be developed for tediagnosis using a small hand-held ultrasound system with an appropriate high frequency transducer. The unique setting will be that the healthcare professional performing the examination may not be a cardiologist or a fully trained echocardiographer, but the examination will be monitored, supervised and guided using telemedicine links which will also allow control of the scanning system settings by the remote supervisor who is an expert Pediatric Cardiologist/echocardiographer.

\The program will assess diagnostic accuracy as the primary outcome variable and time to diagnosis, incidence of unnecessary transport and length of stay during initial hospitalization including transfer when it occurs, as secondary medical outcomes. Diagnosis will be established by testing at a referral center or examination and ultrasound performed by the expert consultant on a follow-up visit occurring at the referral site. In addition to any diagnostic findings of significance which are missed, we will survey and document adverse events in the patient's subsequent course, both medical and social (e.g: parent/baby separation, parental anxiety). Each infant will be followed for 3 months from the time of the initial diagnosis encounter and will be compared to historical controls. Finally, our study will also include a financial outcomes/cost analysis.

**Technical Approach:** This is a prospective, non-randomized, case-control study with measurements obtained at baseline (entry into the study) and three months later. Source data will consist of ultrasound images of the heart transmitted electronically from a remote site to a medical center where they will be read and interpreted. Non-transmitted U/S images and data abstracted from the infant's medical record will be recorded. Data will be obtained at baseline and three months following baseline.

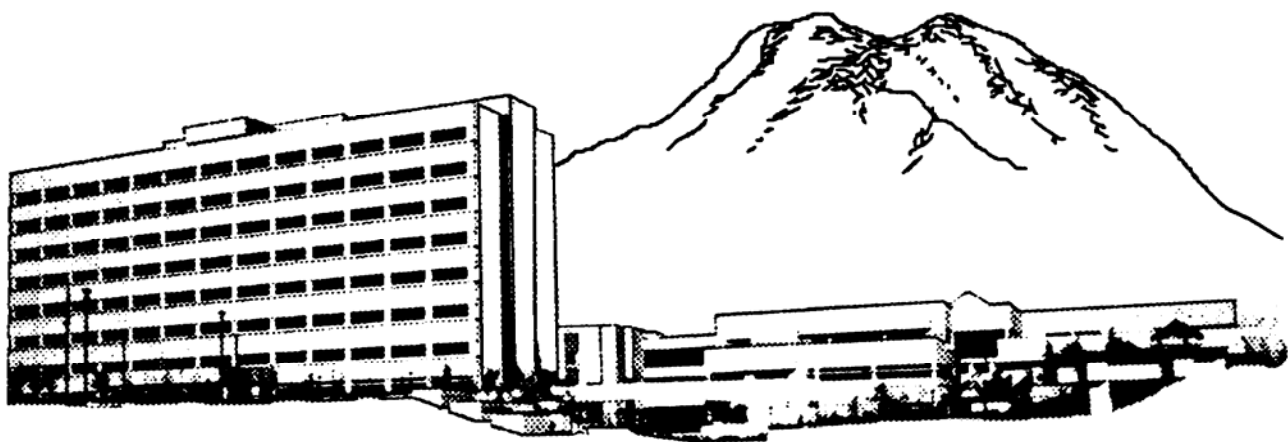
Recruitment and training of health care professionals: two individuals - a pediatrician, family practitioner or obstetrical nurse from each designated participating center will be identified. Initial training in the use of handheld ultrasound systems will occur at MAMC by Drs. Kinney and Puntel and will consist of 2 days of classroom and individual hands-on instruction. A primer on ultrasound instrumentation and methods for performance of cardiac ultrasound will be prepared by Drs. Sahn, Kinney and Puntel. Infants whose families consent will be examined by the attending pediatric cardiologist and have hands-on scanning performed by the trainees under his supervision as the infant's condition allows.

When the portable scanner becomes available for each center and the Telemedicine link is installed and activated, one of the four pediatric cardiologists staffing this program will visit with the trainees at each institution to bring the scanner and operate the telemedicine link, see patients and observe the trainees performing ultrasound examinations, especially in newborns. They will certify on that examination and/or by follow-up observation of Telemedicine observed

studies by those healthcare provider-trainees when they are qualified to activate their site and enroll patients.

Enrollment of patients will begin when all training has been completed and each center has completed its own IRB process. Other care of and testing of the infant will be performed as necessary by the hospital staff and results will be extracted from the patient's medical record. Physical examination, EKG, and/or X-ray will be used, as routinely in a neonatal setting, for identification of potential signs, symptoms, physical examination findings, EKG or radiologic findings of congenital heart disease. Cyanosis will be detected by saturation meter and/or blood gases as necessary. These are part of routine Level II nursery care for newborn infants and will not be altered by the study. These protocols and methods may be specific to the site and documented in the approval of these sites as level 2 or level 3 nurseries.

**Progress:** This protocol remains ongoing and open to enrollment, with 44 subjects enrolled at MAMC for training purposes; 19 in FY06. An additional ten subjects enrolled at Bassett in FY06, all subjects received a TeleECHO diagnosis confirmed 100% with follow-up conventional echocardiography. One patient was diagnosed with Tetralogy of Fallot; underwent heart surgery and is doing well. Twelve TeleECHO training sessions have been completed and 17 doctors trained; three sessions and seven doctors in FY06. Doctors Kinney, Puntel, and Sahn are now privileged to practice telemedicine at all sites except Yukon. All sites, except Yukon, have received the necessary medical equipment for the study and arrangement are beginning to swap out equipment per CRADA/SOW. At this time Bassett, Weed, American Native, Elmendorf, and Bayne-Jones have received IRB approval. Blanchfield will resubmit to the IRB once a new PI completes all requirements. Oak Harbor and Bremerton's protocol is scheduled for another review December 13, 2006 at Naval Medical Center San Diego. Yukon is still on hold due to staff constraints. HSRRB is currently reviewing all IRB approved protocols. Madigan, Bassett, Weed, American Native, and Bremerton have received approvals to connect to local area networks.



# **Detail Summary Sheets**

Department of Pharmacy

### Detail Summary Sheet

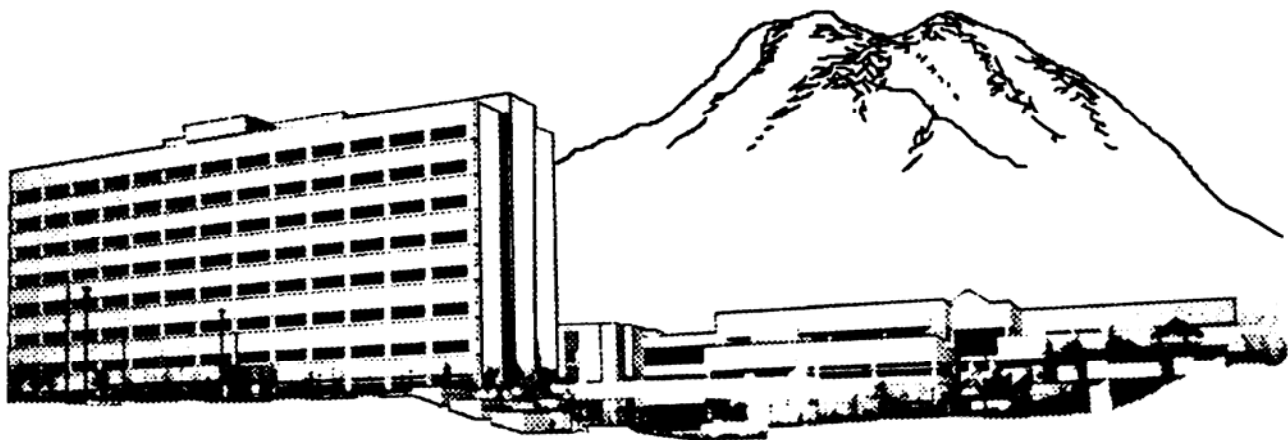
<b>Date:</b> 30 Sep 06	<b>Number:</b> 206092	<b>Status:</b> Completed
<b>Title:</b> Assessment of LDL-Cholesterol Goal Attainment Among Patients at a Very High Risk For Secondary Cardiovascular Events in a Pharmacist-Managed Lipid Clinic		
<b>Principal Investigator:</b> Helen S. Booth, PharmD		
<b>Department:</b> Pharmacy	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Emily V. Leaf, PharmD; Terri G Foster, MA, R.Ph		
<b>Start - Completion:</b> 5/22/2006 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To identify patients at very high risk for secondary cardiovascular events who are unable to attain the newly recommended LDL-cholesterol goal, and to determine the reasons for them not being able to attain their goal.

**Technical Approach:** All patients treated by Madigan Army Medical Center Internal Medicine Lipid Clinic during the study period will be considered for analysis. Internal Medicine Lipid Clinic's Access™ database and the health system's electronic medical record system (AHLTA, ICDB, CHCS) will be used for data collection (patient age, gender, cardiovascular risk factors, LDL-cholesterol level, anti-lipid medication therapy, and reported adverse medication events). Excel™ database will be used to maintain collected data. Patients meeting the inclusion criteria will be identified from the data collection and chart reviews conducted on patients meeting the inclusion criteria. The number of patients identified to be at very high risk for secondary cardiovascular events, the percentage of patients attaining their new LDL-cholesterol goal, medications utilized to attain the goal, and the documented reasons for patients not being able to attain the goal will be reported.

**Progress:** A total of 145 patients were identified to have LDL-C goal of < 70. Seventy-five patients have reached their goal and 70 patients have not reached their goal. Of 75 patients who reached their goal, 41 % was on a statin monotherapy, 3% on other monotherapy, 1% on no medications, and the rest of patients were on a combination therapy. Of 70 patients who did not reach their goal, 63% were in titration phase, 26% had no further treatment options, 10% were lost to follow-up, and 1% was non-compliant. This data was presented at American Society of Health-Systems Pharmacists Summer Meeting 2006.





## **Detail Summary Sheets**

Department of Preventive Medicine

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206056	<b>Status:</b> Completed
<b>Title:</b> Will Power: Is Personal Motivation Associated with Retention in the Army?		
<b>Principal Investigator:</b> CPT Hieu V. Hoang, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Andrew R. Wiesen, MC		
<b>Start - Completion:</b> 1/31/2006 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the association between personal motivation and retention in the Army among Soldiers processed through the Physical Disability Evaluation System.

**Technical Approach:** Cases will be randomly selected from Fort Lewis' electronic archive database for years 2001-2005 and self-identifiers used to match subjects with their paper records. Once the study is completed, self-identifier information will be omitted from the database. A limited database will be constructed for this study to include subjects' sex, age, marital status, rank, MOS, LOS, AD or reserve status, medical diagnosis, and motivation.

**Progress:** This protocol was reported completed in June 2006. The Medical Board is an administrative process whereby Soldiers with a medical disability are evaluated to determine fitness for duty. This cohort study attempted to better understand the role of personal motivation and its associate with retention in the Army. We postulated that personal motivation is positively correlated with retention. Logistic regression was used to evaluate predictors of retention in Soldiers with a disability undergoing the medical board process. Self-expressed motivation as measured by a single question was the strongest predictor of fitness determination. Motivation was highly influential in 6 cases where the PEB had recommended separation, however all 6 cases indicated a desire to remain on active duty and were found fit at the end. In addition, older age, active duty status, MOS of combat support service, and medical diagnosis were found to be statistically significant predictors of retention. It is difficult to say if the studied question truly captures one's motivation, and research is warranted to better assess motivation more accurately.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206066	<b>Status:</b> Completed
<b>Title:</b> Self Identification as a Predictor of Subsequent Mental Health Diagnosis		
<b>Principal Investigator:</b> LTC Victoria R. Hughes, MC		
<b>Department:</b> Preventive Medicine	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 3/22/2006 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if an association exists between self-identification of a mental health concern and the diagnosis of a psychiatric disorder by a psychiatrist or psychologist among Soldiers returning from Operation Iraqi Freedom (OIF).

**Technical Approach:** All Soldiers with 1-25 Stryker Brigade returning from OIF, will be followed to see if at any time during the 5 month (October 2005 to March 30, 2006) post-deployment timeframe they were diagnosed with any of the following specific psychiatric diagnosis [International Classification for Diseases-9th edition] (ICD-9) code(s): adjustment disorder (309, 309.0 -.9), PTSD (309.81), depression (296.2, 296.3 300.4, 311), acute stress disorder (308, 308.0 to .3), anxiety/panic attacks (300.00, 300.01, 300.02, 330.21) and suicidal ideation (300.9) by a provider specifically trained in the area of behavioral/mental health i.e. psychologist or psychiatrist. MAMC Health Outcomes Management Division will provide the dates for the following: completion of post-deployment health assessment (DD 2796), SWAPP and the psychiatric diagnosis.

**Progress:** Results: Of the original 3,151 in the Brigade that returned from Operation Iraqi Freedom (OIF), 250 (8%) were eliminated because they had been previously diagnosed with a mental health illness. This left 2,901 to be in the study group to take the initial post deployment health risk assessment (PDHRA) upon return from OIF. Of these 2,901, just over 57% (1,672) remained on the military installation for the entire 14 month study period. The median age was 26; the most common age was 24, with an age range of 19 to 54. Fifty percent were white, and nearly 37% were single. A majority of the Soldiers were enlisted (86%), with a high school education or less (57%) and only 4% were female. Demographic information that was not completed by the Soldiers on the questionnaires is labeled as unspecified in their respective categories. After completion of the Post Deployment Health Risk Assessment (PDHRA), 33 (2.0%) Soldiers were referred to see a mental health provider. Of those referred, 7 (21.2%) were diagnosed with a mental health illness and 26 (78.8%) were not diagnosed with a mental health illness. Of the 1,639 (98.0%) who had not indicated a mental health concern and therefore had not been referred to see a mental health provider 108 (6.6%) were later diagnosed with a mental health illness, and 1,531 (93.4%) were not diagnosed during the 14 month study period at the military installation's medical facility. This study looked at the six most common mental health diagnoses diagnosed in those who have had war/combat-zone experience, a total of 115 diagnoses made from October 2004 to December 2005. Adjustment disorder was diagnosed in 47 Soldiers, depression in 26, anxiety/panic attacks in 25, PTSD in 10, and acute stress reaction in 7. Of the 10 Soldiers diagnosed with PTSD, none were self identified. Suicidal ideation was not self identified by any of the Soldiers, nor was suicidal ideation diagnosed in any of the Soldiers.

**Conclusions:** This study shows that early self identification of mental health concerns is not predictive of a clinical diagnosis from a mental health provider at a military clinic within 14 months. There were more mental health diagnoses made for those who did not initially self identify with having a mental health concern when taking the PDHRA. This suggests the idea that some mental health symptoms develop over time after a traumatic experience. A second, later,

assessment may need to be done to improve its predictive value. The mental health diagnoses made were relatively rare; 115 (6.9%) out of a cohort of 1,672. These results are low compared to the 12% diagnosed in Hoge's study published March 2006. The number of positive self identifications for a mental health concern is minimal at 33, compared to the number of non self identifications of a mental health concern at 1,639. Single Soldiers appear to be more at risk of being diagnosed with a mental health illness. Being married possibly helps a soldier in coping with mental health concerns. Only 5% of married Soldiers had a positive mental health diagnosis, compared to 9% of single Soldiers and 95% married Soldiers were not diagnosed with a mental health illness. Marriage most likely provides for a good support system that is accessible, while those who are not married may have support systems that are less easily available. None of the Soldiers diagnosed with PTSD were initially self identified at the time the PDHRA was completed. This is most likely the case because it may take up to several months after the traumatic event for someone to actually develop signs and symptoms of PTSD. It is also possible that mental health providers do not want to give a soldier a mental health diagnosis right away.

On site mental health diagnoses are probably the tip of iceberg for post- combat mental health illness, given how few diagnoses were made. Assessments done immediately upon return miss many Soldiers. Signs and symptoms for post traumatic mental health illnesses do not manifest immediately. Mobility of the cohort limited the ability to have continuity of care. Many Soldiers were not available to take the second health risk assessment given at 3 to 6 months after return from OIF. This may have prevented some Soldiers from self identifying a mental concern and possibly from even realizing that maybe they were having symptoms when asked specific mental health questions. Of those 1,672 around for the entire 14 months, only 799 took the Health Risk Assessment II. Why the compliance was so low in taking the second assessment is not completely clear. Several possible reasons are that Soldiers were out in the field training, that they were on vacation or sick, or that they just did not want to go to take the assessment. Once it was noticed that the numbers were low, those responsible for conducting the assessment decided to take the assessment to the Soldiers. Effective mental health programs for military service members are essential. The military command needs to be aware and responsive to young, single, low ranking Soldiers returning from a war/combat-zone who may experience more mental health issues than other Soldiers.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206074	<b>Status:</b> Completed
<b>Title:</b> Military Rank as a Risk Factor for Type 2 Diabetes in Military Spouses		
<b>Principal Investigator:</b> LTC Carol A. Moores, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 3/30/2006 - May 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine whether rank is associated with the likelihood of type 2 diabetes mellitus in the spouses of active duty military.

**Technical Approach:** This study will generate a Case Group of 400 spouses with ICD-9 codes consistent with Type 2 Diabetes and generate a Control Group of 400 spouses that do not have an ICD-9 code consistent with any type of diabetes. (Both groups have been seen in primary care within the past 12 months.) Variables to be generated include age, gender, sponsor rank, number of people in family, race/ethnicity. Outpatient records will be reviewed for confirmation that the provider(s) have given a working diagnosis of Type 2 diabetes (rather than Type 1 Diabetes or other diagnosis). A subject will be excluded if the record does not indicate Type 2 Diabetes. All records will also be reviewed for BMI and tobacco use information. Data will be summarized using descriptive statistics. Data will be analyzed using logistic regression. Modeling will be used to determine the most important predictive variables and the relationships between those variables.

**Progress:** This protocol was reported as completed in June 2006. A chart review was conducted of 840 health records with 680 meeting the inclusion criteria. Results showed no evidence of an association between the rank of an active duty military service member and the likelihood of type 2 diabetes in the spouse.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206033	<b>Status:</b> Completed
<b>Title:</b> Hazards to Hearing and Threshold Shifts: The Results of Deployment to a Combat Environment		
<b>Principal Investigator:</b> MAJ Troy W. Ross, MC		
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> William Daniell, MD; LTC Andrew R. Wiesen, MC		
<b>Start - Completion:</b> 12/14/2005 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** This proposed study will determine the incidence of hearing loss in the cohort over the period of deployment, use a survey tool to establish correlations between hearing hazards and measured threshold shifts, use a survey to establish the patterns of use of hearing protection and use the findings of this study to improve the Military's hearing conservation program.

**Technical Approach:** Baseline screening audiograms will be obtained on 4000 active duty Soldiers prior to deployment and follow up exams will be completed after their return. Additionally, a questionnaire will be administered to the group as part of their post deployment screening to determine how hearing protection was used, the noise hazards experienced, and what ototoxic exposures the soldiers may have had. The incidence of hearing loss will be correlated to protection measures that were used and hearing hazards that were experienced.

**Progress:** This protocol was reported completed in June 2006, with 3,231 Soldiers meeting inclusion criteria and identified as members of the 1st Stryker Brigade during the post deployment health screening. Of those, 2,370 were offered surveys, and 1,176 surveys were returned (49% response). The cohort was overwhelmingly male and about half were in direct combat occupations. The length of service categories showed an unequal distribution with relatively more Soldiers in the earlier years of service, but this corresponds to the distribution of the general Army population.

Results: 623 members of the cohort were identified as having an STS. This yields an annual incidence of 19.2%. The STS rate was similar for male and female soldiers, slightly higher for combat soldiers than those in support positions, and progressively lower with longer length of service. The STS rates ranged from 15.4% to 21.8% in the eight non-combat jobs categories, but the differences were not statistically significant

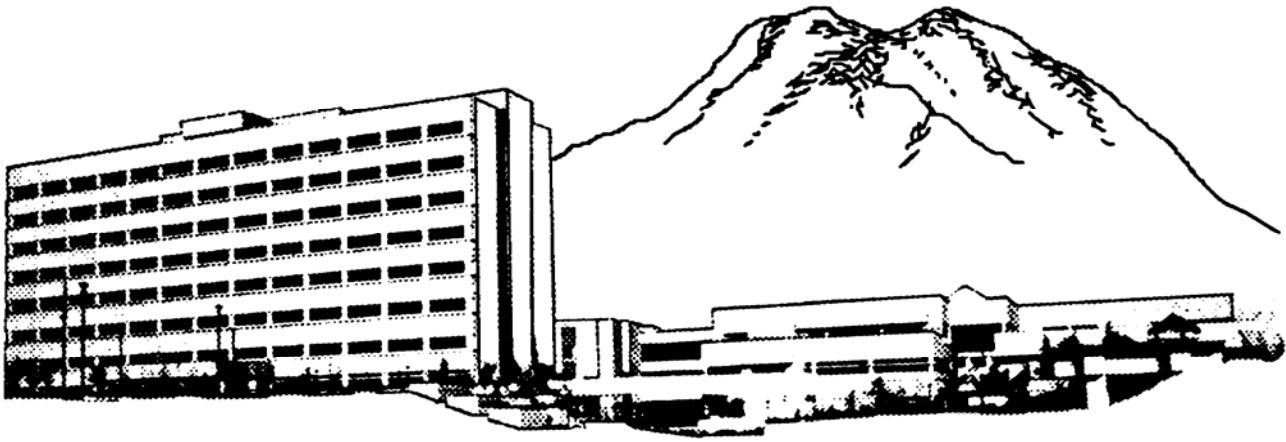
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 205099	<b>Status:</b> Ongoing
<b>Title:</b> CD4+ T Cell Epitope Identification for Protective Antigen of Bacillus Anthracis			
<b>Principal Investigator:</b> LTC Andrew R. Wiesen, MC			
<b>Department:</b> Preventive Medicine		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Michele A. Soltis, MC; William W. Kwok, Ph.D.			
<b>Start - Completion:</b> 12/13/2005 - Mar 2007		<b>Funding:</b> Benaroya Research Institute via CRADA	<b>Periodic Review:</b> 6/20/2006

**Study Objective:** To describe CD4+ T cell epitopes of the Protective Antigen of Bacillus.

**Technical Approach:** This is a purely descriptive, basic science study, intended to further understanding of how the human immune system responds to anthrax vaccine. Up to 30 individuals who have received at least 3 doses of anthrax vaccine will be asked to undergo HLA typing (cheek swab). Those with a common HLA type will be asked to give a sample of blood (maximum of 120 cc) for epitope mapping of CD4+ cells. The participants will be drawn from the Fort Lewis active duty and former active duty population. Data analysis will be from flow cytometry methods. As there is no formal hypothesis testing, there will be no formal statistical analysis.

**Progress:** This protocol remains open to enrollment with 35 patients enrolled at MAMC; 26 subjects had HLA typing completed and nine have HLA typing in progress. Of the 26 who had HLA typing completed, one was HLA non-compatible, two departed the Fort Lewis area prior to blood draws, and two blood draws are pending. Of the 21 subjects who had blood drawn for the study, six were asked to submit a second sample, and three were asked to submit a third sample. There have been no significant adverse events during the study. One subject suffered a momentary loss of consciousness during the blood draw, but recovered uneventfully. Recruitment continues. There has not yet been a patient with DR-8 antigen enrolled in the study.



# **Detail Summary Sheets**

## **Department of Psychiatry**



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204089	<b>Status:</b> Ongoing
<b>Title:</b> A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced Nightmares and Sleep Disturbance		
<b>Principal Investigator:</b> LTC Kris A. Peterson, MC		
<b>Department:</b> Psychiatry	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Christine M. Daly, MC; LTC Michael E. Doyle, MC; Larry G. Knauss, Ph.D.; Elaine R. Peskind, M.D.; Miles M. McFall, Ph.D.; Murray A. Raskind, M.D.; David J Hoff, PA-C; Kimberly L Hart, PA-C; Michele Klevens, MA; James O'Connell; Hollie A Holmes; Kirsten Rohde, RN, BSN		
<b>Start - Completion:</b> 10/29/2004 - Sep 2008	<b>Funding:</b> VA via MIPR	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** The primary goal of this study is to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist prazosin (available commercially since 1972) compared to placebo for combat stress-related nightmares, sleep disturbance and overall function in recently combat-exposed returnees from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). A secondary goal is to evaluate the effects of the selective serotonin reuptake inhibitor (SSRI) paroxetine on behavioral symptoms and overall function in this population.

**Technical Approach:** Sample Population/Sample Size includes 90 male and female returning troops from OIF and OEF who manifest persistent combat stress-related nightmares and sleep disturbance. Methods: responses of combat stress-related nightmares, sleep disturbance, and over all stress-related symptom severity will be compared among groups randomized to the alpha-1 adrenergic antagonist prazosin, the SSRI paroxetine, and placebo in a 12-week, double-blind study. Outcome Variables: Clinician-Administered PTSD Scale (CAPS) item 2 "recurrent distressing dreams," item 13 "disturbed sleep," and total CAPS score; Pittsburgh Sleep Quality Inventory; Clinical Global Impression of Change; Hamilton-Depression Rating Scale total scores. Data Analysis Plan: Data will be analyzed for significant differences in outcome variables among treatment groups using generalized estimating equations.

**Progress:** This protocol remains open to enrollment. During FY06, 23 subjects were randomized; thirteen were screen failures (eight no-showed for screen). Of the 23 subjects randomized, one is currently participating, eight completers (2-prazosin, 3-paroxetine, 3-placebo), fourteen non-completers (eight lack of compliance, three time/scheduling conflicts, one deployed, one worsening symptoms, one terminated by investigator at baseline). There were no adverse events reported.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206011	<b>Status:</b> Ongoing
<b>Title:</b> Prazosin for the Treatment of Trauma Nightmares in PTSD		
<b>Principal Investigator:</b> LTC Kris A. Peterson, MC		
<b>Department:</b> Psychiatry	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Murray A. Raskind, M.D.; Elaine R. Peskind, M.D.; Miles M. McFall, Ph.D.; Larry G. Knauss, Ph.D.; Bradford L. Felker, MD; Jessica W. Cook, PhD		
<b>Start - Completion:</b> 12/22/2005 - Sep 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/24/2006

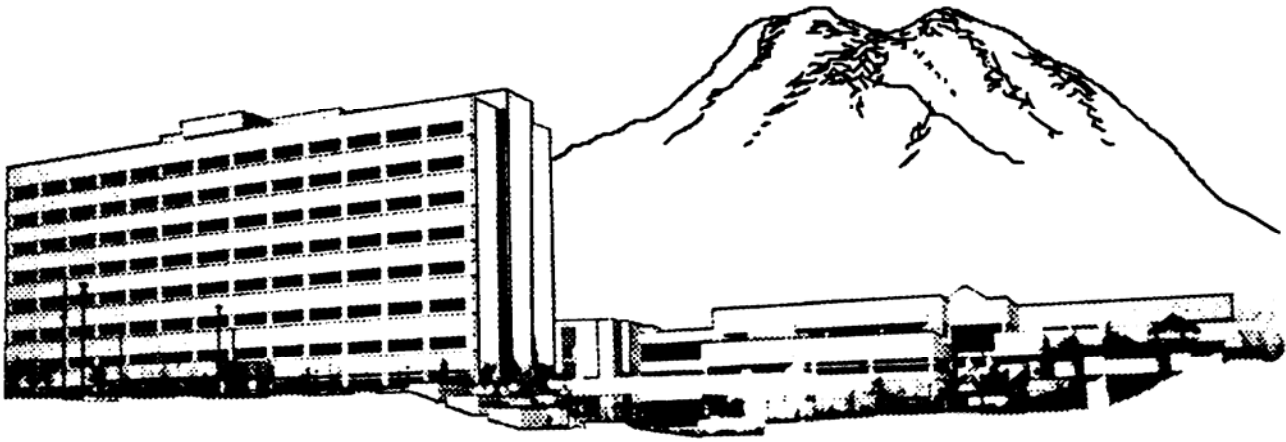
**Study Objective:** The primary goal of this study is to evaluate the efficacy and tolerability of the alpha-1 adrenergic antagonist prazosin (available commercially since 1972) compared to placebo for combat stress-related nightmares, sleep disturbance and overall function in recently combat-exposed returnees from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF).

**Technical Approach:** Men and women (120 subjects) with both persistent (> one month duration) troublesome combat stress-related nightmares (CAPS "recurrent distressing dreams" item 5 [maximum score = 8]) and sleep disturbance (CAPS "difficulty falling or staying asleep" item 5 out of a maximum score of 8) who are in good general health and are not taking exclusionary medications are eligible for this study. This is a double-blind, placebo-controlled treatment study of prazosin in combat-exposed persons who have trauma-associated nightmares and sleep disturbance. After a titration period (1-8 weeks in duration) to reach "optimum" dose (up to a maximum of 25 mg/day of prazosin for subjects who weigh less than 250 lbs and 30mg/day of prazosin for subjects who weigh more than 250 lbs), subjects will come to the clinic every two weeks to undergo efficacy evaluation. After the treatment period, the blind will be broken and subjects will be referred to their primary mental health provider for further treatment. Subjects will come in to the clinic for follow-up visits 12 and 26 weeks after the treatment period ends.

Outcome measures will include Clinical Global Impression of Change (CGIC), Recurrent Distressing Dreams and Difficulty Falling and Staying Asleep items of the Clinician-Administered PTSD Scale (CAPS), PTSD Dream Rating Scale (PDRS), Nightmare Frequency Questionnaire (NFQ), Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI). Depression and quality of life will also be assessed with the Hamilton Depression Rating Scale (HAM-D) and Quality of Life Index (QOLI). The primary intent-to-treat (ITT) efficacy assessment will compare the prazosin and placebo group's CGIC scores at 8 weeks. Since response is not anticipated to be progressive, any missing observations will be imputed using the last observation carried forward (LOCF) procedure. The CAPS Recurrent Distressing Dreams and Difficulty Falling or Staying Asleep items, total CAPS, Mississippi Scale, PSQI, ISI, PDRS, NFQ, Ham-D, and QOLI item will be analyzed as a continuous response measure. Rates of change in response measures will be evaluated according to ITT between the prazosin and placebo groups using an analysis of covariance model with the 8-week values as the response measure and baseline measure as a covariate along with any potential confounding variables. The median time to study discontinuation (in those patients who drop out secondary to unacceptable adverse effects) will be compared between the two treatment groups using the Cox proportional hazards model. Frequency of individual adverse event occurrence will be compared by chi square and adverse event severity by unpaired t-test between prazosin and placebo conditions to estimate the clinical significance of potential prazosin adverse effects.

**Progress:** This protocol remains open to patient entry, with twelve subjects consented during FY06. Two subjects did not begin study medication after randomization (the blind was not broken in these two cases). Three subjects (2-prazosin, 1-placebo) were removed from the study due to

compliance issues. One subject (placebo) withdrew at Week 04 due to relocation. One subject (prazosin) withdrew at Week 08 due to relocation; and although blinded portion of the study was complete, the subject was not seen for follow-up visits. Two subjects (2-placebos) completed the blinded portion of the study and are currently active in follow-up. Recruitment is ongoing.



# **Detail Summary Sheets**

Department of Psychology

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206062	<b>Status:</b> Ongoing
<b>Title:</b> Military Readiness Risks: Leader Perspectives Impact on Mandatory Addiction Referrals		
<b>Principal Investigator:</b> Jolee N. Darnell, MSW, LICSW, CDP		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Lori A. Loan, RNC, Ph.D.; Brenda M. Wilson, MS, LPA, CDP; Ross A. Echterling, BS, CDP; Joseph D. Darnell, BA		
<b>Start - Completion:</b> 6/10/0063 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The goal of the research is to determine whether there are other interventions or education that could be used to target and improve the referral rates and ultimately military readiness.

**Technical Approach:** This proposal uses a qualitative research method approach to examine questions related to the impact of leader attitudes and operational tempos on completion of mandatory substance abuse referrals. Action research methods will be used, including ex post facto review of existing data and interviews and focus groups with key stakeholders (Active Duty Fort Lewis military leaders at the levels of platoon, company, battalion, and brigade). The researcher will coordinate with the First Corps Surgeon's office and each Brigade Surgeon's office to recruit focus group and individual interview volunteers from each Brigade size unit at the installation. Recruitment requests will be made through the process of Officer Professional Development (OPD) and Non-Commissioned Officer Professional Development (NCOPD) during required training on health and health care related topics.

Following documented informed consent, the study will use interviews and focus group discussions to generate information for the research questions. Discussion topics will include: participant understanding of regulatory referral requirements, participant philosophy about alcohol and drug use in the military; participant understanding of substance abuse and dependence; perspectives about positive and negative aspects of the Army's mandatory substance abuse referral program; participant perspectives on data trends; participant perspectives about relationships between military mission requirements and mandatory substance abuse referral processes. Before focus groups and interviews are conducted, specific dialogue will be validated for appropriateness by an expert panel of line leaders and professionals involved in the referral process. The goal is to get the experts to provide guidance and critique of the specific discussion topics to be used in the focus groups and interviews.

**Progress:** Four individual interviews have been conducted. Three interviews and one focus group have been scheduled 14 November 2006. The study has shifted to more interviews and less focus groups, since military operations schedules during the summer months had an impact on ability to schedule focus groups. The goal is to interview 15-30 military leaders individually or in groups about their perspectives on substance abuse referral procedures. Transcription of interviews conducted to date is reflecting some expected responses as well as perspectives not clear from data analysis reviews prior to the interviews. One perspective that has emerged reflects the level of knowledge or training received by unit leadership about requirements and benefits of using the substance abuse referral process. Group and individual interviews/data collection is projected to be completed by 1 December 2006. Transcription and preliminary data analysis is projected to be completed by 31 Dec 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205019	<b>Status:</b> Ongoing
<b>Title:</b> Theory-Guided Anticipatory Guidance		
<b>Principal Investigator:</b> Patti L. Johnson, Ph.D.		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Christine Moon, PhD		
<b>Start - Completion:</b> 12/3/2004 - Oct 2005	<b>Funding:</b> UW/PLU	<b>Periodic Review:</b> 11/30/2006

**Study Objective:** The objective is to test the application of the prevailing psychological theory of persuasion on information delivery to mothers of young infants.

**Technical Approach:** This study will test the use of the Elaboration Likelihood Model (ELM) of persuasion on attitude change of 200 mothers of newborn infants regarding early shared reading with their infants. The two independent variables are 1) two levels of participants' live birth (para status and 2) two formats of a brief education intervention. The education intervention will be administered during the last 10 minutes of a 20-minute session to be scheduled after the daily Mother/Baby Unit discharge class. During the first 10 minutes, informed consent will be obtained and three brief questionnaires will be completed: a personal information questionnaire, the Sensations during Pregnancy and Life Events Questionnaire, and a questionnaire on attitudes about early shared reading. The effect of intervention will be assessed two months later by re-administering the questionnaire on attitudes about early shared reading. Para status is a marker for level of distraction from parenting the new baby, important for ELM application. Verification of level of distraction will be made by using the Sensations during Pregnancy and Life Events Questionnaire.

At the conclusion of data collection, there will be 40 mothers in each of the 4 intervention groups (2 para statuses X 2 formats.) A control group (n=40) will receive general information on speech/language development. The dependent variable will be difference scores on the pre- and post-intervention questionnaires on attitude about early shared reading, and the difference scores will be analyzed using analysis of variance. It is predicted that there will be a statistically significant interaction effect between para status and intervention format. Further, difference scores of both intervention groups will be higher than control group scores. Results of the experiment are expected to inform the practice of information delivery to patients, specifically in anticipatory guidance in pediatrics.

**Progress:** This protocol remains open to enrollment with 149 participants enrolled to date, which represent half of the 300 participants planned for this study. Virtually no data were collected since December 2005 due to changes in personnel and lack of research funding for the project. Personnel will become available for the project in January 2007 and data collection will resume.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206088	<b>Status:</b> Ongoing
<b>Title:</b> Exposure to Death and Dying and Mental Health Response in Operation Iraqi		
<b>Principal Investigator:</b> Barbara A. Lucenko, PhD		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Shira Maguen, PhD; COL Gregory A. Gahm, MS		
<b>Start - Completion:</b> 5/8/2006 - May 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To test a model demonstrating the relationship between exposure to death and dying, mental health outcome, and functional impact following deployment to Iraq.

**Technical Approach:** The Health Risk Appraisal II (HRA-II) is administered 90 days post-deployment. Soldiers completed an automated version of the HRA-II in groups scheduled according to specific Active Duty units. Groups were reportedly scheduled according to unit re-deployment status. The screening may have occurred at any point between 60 and 120 days after returning from deployment, although the typical timeframe has been reported as between 60-90 days. A data transfer process serves to populate a secure Oracle database housed within the Army Behavioral Health Technology Office. Algorithms written into software score the clinical scales and generate reports for Behavioral Health (BH) routing and provider use. All soldiers are then seen by a BH provider on site and follow up clinical referrals are made based on both screening and interviews. Prior to analyses for this project, appropriate fields from the database will be copied stripped of all identifying information (name, social security number, and contact information). The relevant variables outlined in this proposal will be sent to the San Francisco VA Medical Center for the specified data analysis. Dr. Maguen will not have access to any of the identifying information (names and social security numbers, and contact information) at any point during the study. Also, the data will continue to be owned by MAMC.

**Progress:** A data set was finalized, de-identified, and forwarded to Dr. Maguen for analyses. The protocol remains ongoing as analyses are still in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206118	<b>Status:</b> Ongoing
<b>Title:</b> User Centered Design Feedback for the Virtual Iraq		
<b>Principal Investigator:</b> CPT Greg M. Reger, MS		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Gregory A. Gahm, MS; Mark A. Reger, PhD; John L. Miller, MD; Barbara A. Lucenko, PhD; Albert A Rizzo, PhD; CPT Roberta L. Shepard, MC; Robert D. Swanson, M.A.		
<b>Start - Completion:</b> 10/19/2006 - Jul 2007	<b>Funding:</b> TATRC	<b>Periodic Review:</b> N/A

**Study Objective:** To obtain user-centered design feedback from healthy, non-patient soldiers to guide the project development of a virtual reality application (VR Iraq) intended for future use to treat a wide range of possible traumatic combat experiences.

**Technical Approach:** Following consent, Soldiers will complete a brief demographic questionnaire and PTSD Checklist, which is a validated PTSD screening tool. The consenting investigator will review these documents and ensure that the participant meets inclusion/exclusion criteria. In the case that the participant self-reports significant levels of trauma related symptomatology, the investigator will discontinue formal participation in the project and will offer to discuss their responses on the survey and escort participants to a private location to talk (e.g., Behavioral Health Clinic or Soldier Readiness Service) to discuss options for referral and treatment, if indicated. Participants who meet inclusion/exclusion criteria will utilize the two VR scenarios. The current city scenario has the appearance of a desolate set of low populated streets comprising old buildings, ramshackle apartments, warehouses, a mosque, factories, and junkyards. The second scenario is a convoy scenario in which the user navigates down paved and dirt desert roadways with occasional areas of vegetation, battle wreckage, and debris. As soldiers navigate through these environments, the investigator will activate currently available trigger stimuli. Currently, the VR Iraq allows the controller to introduce audio triggers (i.e., incoming mortars, weapons fire, voices, wind, etc.) and audiovisual triggers (e.g., helicopter flyovers). Total time utilizing the VR Iraq will be approximately 5 minutes.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 22 August 2006. Final approval was granted 19 October 2006.



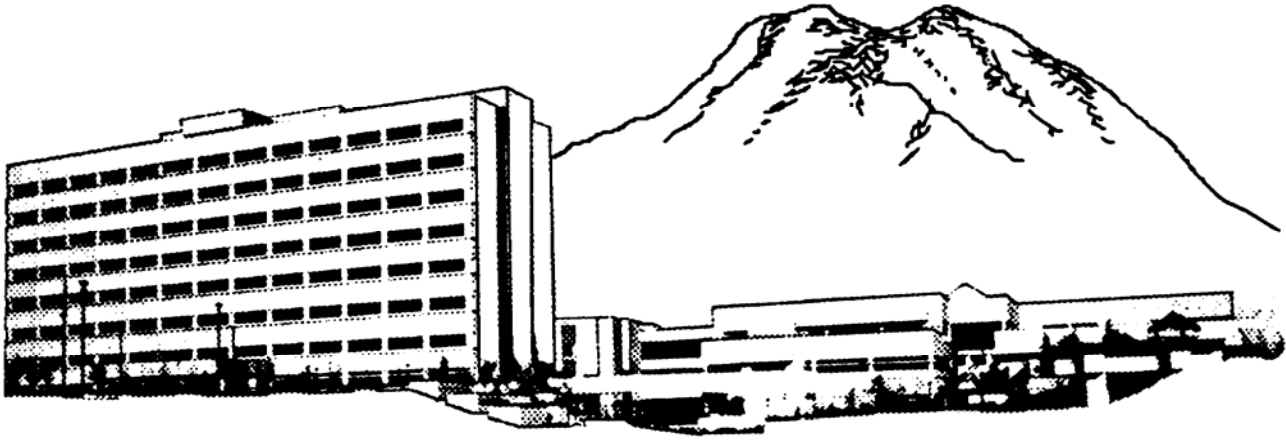
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206077	<b>Status:</b> Ongoing
<b>Title:</b> Army Suicide Event Report: Data Analysis		
<b>Principal Investigator:</b> Mark A. Reger, PhD		
<b>Department:</b> Psychology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Gregory A. Gahm, MS; Barbara A. Lucenko, PhD		
<b>Start - Completion:</b> 4/10/2006 - Mar 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To establish an effective and efficient model of risk assessment for suicide, suicide ideation, and suicide attempts using existing data from the Army Suicide Event Report (ASER).

**Technical Approach:** This study is a retrospective review and exploratory analysis of Soldiers for whom ASER data exists. Initial review reveals 742 records as of November 2005. The study will track suicide behavior for 2005-2007, using exploratory analyses to detect trends and risk and protective factors.

**Progress:** A total of 1,128 Army Suicide Event Reports (ASER) have been submitted during FY06, out of a total 1,616 that are in the database. Data collection continues, analyses have not been conducted for this protocol to date.



# Detail Summary Sheets

Department of Radiology

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202117	<b>Status:</b> Ongoing
<b>Title:</b> Intravenous Administration of 131 I-6-B Iodomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging		
<b>Principal Investigator:</b> LTC Antonio G. Balingit, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Deborah E. Floyd, MS; COL (Ret) Jerome L. Billingsley, MD; Jane E. Besich-Carter, BS, BCNP		
<b>Start - Completion:</b> 1/7/2004 - Jul 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** Clinical evaluation of NP-59 as a diagnostic agent for the detection of adrenocortical disorders.

**Technical Approach:** The drug to be used in this study, NP-59, is investigational and will be used under IND number 12605, which is held by the University of Michigan. This study will be performed in humans of either sex only after complete evaluation by the Endocrinology Service of MAMC. All female patients between the ages of twelve and fifty-five will have a serum B-HCG determination except those who had a hysterectomy. Pregnant or lactating patients will be excluded. This agent will be administered to children less than 18 years of age only for exceptional reasons with the approval of the Chief, Nuclear Medicine Service and Chief, Pediatric Endocrinology Service and only after other alternative procedures are determined to be inappropriate. Ideally, studies in women of childbearing capability are performed during the first 10 days post-menses. NP-59 will be obtained in pharmaceutical form from the University of Michigan Nuclear Pharmacy. In house quality control, including determination of radionuclidic and radiochemical purity, will be performed on all shipments of NP-59 prior to human use. NP-59 will be administered by slow intravenous injection with a dose of 2mCi in adults, 15 UCi/kg in children except where the benefit to risk ratio warrants a higher dose. Under no circumstances will more than 2.2 mCi be administered. Lugol's solution, 5 drops twice daily starting one day before injection and continuing for two weeks, will be used to block thyroid uptake of radionuclide. Planar and SPECT images will be obtained on the 3rd, 4th and 5th days after injection using a dual detector scintillation camera connected to an on-line computer. Studies will be performed in accordance with the protocol "<sup>131</sup>I-6-B iodomethylnorcholesterol." Informed consent will be obtained prior to entry into the study.

**Progress:** No patients have been enrolled. The radiopharmaceutical is an 'orphan' drug and infrequently utilized therefore has not been FDA approved. It can be procured only as an IND. Nuclear Medicine Service has to keep a protocol ongoing in order to utilize the drug as the need arises.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206053	<b>Status:</b> Ongoing
<b>Title:</b> NSABP B-39 / RTOG 0413 A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I or II Breast Cancer		
<b>Principal Investigator:</b> LTC William B. Reece, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC John B. Halligan, MC; MAJ Joseph P. Brooks, MC; MAJ Jasmine T. Daniels, MC; MAJ Angela G. Mysliwiec, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 6/5/2006 - Feb 2011	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objective is to determine whether partial breast irradiation (PBI) limited to the region of the tumor bed following lumpectomy provides equivalent local tumor control in the breast compared to conventional whole breast irradiation (WBI) in the local management of early stage breast cancer.

Secondary objectives are (1) to compare overall survival, recurrence-free survival, and distant disease-free survival between women receiving PBI and WBI, (2) to determine whether PBI delivered on 5 treatment days over a period of 5 to 10 days can provide a comparable cosmetic results to WBI, (3) to determine if PBI produces less fatigue and treatment-related symptoms compared to WBI, (4) to determine if perceived convenience of care is greater for women receiving PBI compared to women receiving WBI and (5) to compare acute and late toxicities between the radiation therapy regimens.

**Technical Approach:** This Phase III, randomized trial will enroll patients with stage 0 (DCIS) or stage I or II invasive adenocarcinoma of the breast with no evidence of metastatic disease who have undergone lumpectomy with cancer-free margins, and have no more than 3 positive axillary nodes. Patients will be stratified according to disease stage, menopausal status, hormone receptor status, and intention to receive chemotherapy. Following stratification, patients will be randomized to receive WBI or PBI. WBI for this study will be standard techniques delivered over 5 to 7 weeks. PBI will utilize the technologies of high dose-rate multi-catheter brachytherapy, high dose-rate single catheter balloon brachytherapy (MammoSite), and three-dimensional conformal external beam radiation therapy. Patients randomized to receive WBI will receive chemotherapy, if applicable, before their radiation therapy. Patients randomized to PBI will receive radiation therapy before chemotherapy, if applicable. For patients who agree to blood and tissue studies, blood will be submitted after randomization but before therapy begins and tissue blocks will be submitted within 3 months after randomization. Patients will have follow-up visits at end of radiation therapy, 4 weeks, 6 months, 12 months, every 6 months through Year 5, then annually through Year 10. The first 482 patients who are having chemotherapy and the first 482 patients who do not intend to receive chemotherapy will have the option of being included in a QOL and cosmesis study. These patients will have 7 QOL questionnaires to complete during the course of treatment and follow-up, and will have three sets of digital photographs taken of their breasts at baseline, Year 1 and Year 3. RTOG will provide a web-based image management system for sites to upload images as JPEG files. Each site will have restricted access to only their image archive, and once images are uploaded they will only be accessible to NSABP reviewers. The primary statistical endpoint for the study is diagnosis of in-breast tumor recurrence (IBTR). Regional and distant failures and death prior to IBTR will be treated as competing risks. Contralateral breast and non-breast secondary primary cancers will not be considered as competing risks. Secondary endpoints include distant disease-free interval, recurrence-free survival and overall survival.

**Progress:** This protocol is open to patient entry, with no patients enrolled during FY06. A slow down in recently diagnosed early stage breast cancer patients has occurred recently; this protocol will remain ongoing to accrue patients over the next year.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204069	<b>Status:</b> Ongoing
<b>Title:</b> SWOG RTOG 0212, A Phase II/III Randomized Trial of Two Doses (Phase III-Standard vs. High) and Two High Dose Schedules (Phase II-Once vs Twice Daily) for Delivering Prophylactic Cranial Irradiation for Patients With Limited Disease Small Cell Lung Cancer		
<b>Principal Investigator:</b> LTC William B. Reece, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC John B. Halligan, MC		
<b>Start - Completion:</b> 7/20/2004 - May 2007	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 4/10/2006

**Study Objective:** (1) To determine the impact of an increase in the total PCI dose on the incidence of brain metastases at a minimum of 2 years of patient follow up; two PCI dose levels will be compared: 25 Gy (standard dose PCI) versus 36 Gy (high dose PCI) in limited disease small cell lung cancer (LD SCLC) patients in complete remission, whatever the initial treatment. (2) To determine the impact of PCXI dose of overall and disease-free survival; (3) To determine the impact of PCI dose on quality of life and late treatment sequel, 4) To determine the impact of PIC dose and schedule on the incidence of chronic neurotoxicity, and (5) To determine the impact of PCI dose and schedule on quality of life.

**Technical Approach:** About five to seven subjects per year would potentially eligible for this protocol at Madigan Army Medical Center. The protocol randomizes subjects to receive one of three doses of prophylactic cranial irradiation. Arm I subjects receive 2.5 G ray once daily for 10 fractions for a total of 25 G ray. Arm II subjects receive 2.0 G ray once daily for 18 fractions for a total of 36 G ray. Arm III subjects receive 1.5 Gray once daily for 24 fractions for a total of 36 G ray. The study will examine the incidence of brain metastases as the primary end point and assess the cognitive and neurologic side effects of subjects on the above treatment doses and delivery schedules through neurotoxicity/neuropsychological testing. The results of this study may modify the standard dose schedule currently used in the delivery of this critical treatment.

**Progress:** This protocol closed to enrollment with one patient enrolled who continued to be followed at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205134	<b>Status:</b> Ongoing
<b>Title:</b> Clinical Trial and Retrospective Review to Determine the Sensitivity and Specificity of Iminodiacetic Acid Scintigraphy for Fibrolamellar Carcinoma		
<b>Principal Investigator:</b> CPT David C. Semerad, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Antonio G. Balingit, MC; COL (Ret) Jerome L. Billingsley, MD; LTC John D. Statler, MC		
<b>Start - Completion:</b> 1/11/2006 - Jul 2009	<b>Funding:</b> Nuclear Medicine	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To determine the sensitivity and specificity of iminodiacetic acid (IDA) scintigraphy for the detection of fibrolamellar carcinoma presenting as a solitary liver mass with a central scar on CT examination.

**Technical Approach:** Patients at MAMC who have a solitary liver mass with a central scar on CT will undergo IDA scintigraphy in addition to the standard diagnostic algorithm. It is estimated that 12 patients will be studied at MAMC over a 4-year period. The study protocol will also be submitted to IRBs at WRAMC and BAMC. A retrospective analysis of histologically-confirmed FLCs with IDA scintigraphy findings will also be conducted at MAMC, WRAMC, and BAMC. The goal number of total subjects is 80. The sole variable is radiopharmaceutical uptake of the lesion. Data analysis is solely descriptive, i.e. establishing the sensitivity and specificity of IDA scintigraphy for FLC.

**Progress:** This protocol remains open to enrollment, with no subjects enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205051	<b>Status:</b> Ongoing
<b>Title:</b> Carotid Stenosis: Digital Subtraction Angiography, Magnetic Resonance Angiography, and the Evolution of Preoperative Evaluation		
<b>Principal Investigator:</b> LTC John D. Statler, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Joseph A. Ronsivalle, MC; CPT Christopher S. Johnson, MC; CPT Vance Y. Sohn, MC; LTC Benjamin W. Starnes, MC; COL (Ret) Charles A. Andersen, MD; Billinda Tatum, RN, CCRC; Leslie B. Schoneman, PA-C		
<b>Start - Completion:</b> 6/7/2005 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2/28/2006

**Study Objective:** This study will serve as a validation that magnetic resonance angiography (MRA) is no worse than catheter angiography in the evaluation of atherosclerotic disease of the carotid arteries.

**Technical Approach:** All adult MAMC healthcare beneficiaries referred for carotid arteriography (DSA) from vascular surgery clinic will be eligible for participation. If a patient agrees to be enrolled in the study, he/she will be consented during the visit to the vascular surgery clinic. The subject will be scheduled for DSA and MRA at the same time and will undergo both of these exams in the most expeditious order possible. Once the exams have been completed, each subject's DSA will be performed, reviewed and interpreted by one radiologist, and the MRA will be reviewed and interpreted by the other radiologist. The radiologist interpreting the MRA will be blinded to the results of the DSA, and vice-versa. Findings will be recorded on the data sheet. A general comment will be made on the quality of each exam. The images will be evaluated for percent stenosis of the common and internal carotid arteries using NASCET criteria (12) and measured by imaging software. Findings will be made based on standardized imaging criteria. Findings which may alter patient management (near occlusion, plaque ulceration, etc.) will be catalogued. At the conclusion of the review of the MRA and DSA, the results for each subject will be compared. Each subject will receive a grade with respect to the concordance of the two exams. A grade of "no difference" indicates that MRA and DSA concurred with respect to percent stenosis (+ - 10%) of internal and common carotid, and that there was no difference in detection of findings which would alter patient management. A grade of "minor difference" indicates discordance between MRA and DSA with respect to stenoses or associated findings, but that these discrepancies would not affect the decision to operate or the operative approach. A grade of "major difference" indicates discordance between MRA and DSA which would alter patient management or operative approach (discordant stenosis category, associated findings which would alter surgical management).

**Progress:** This protocol remains open to enrollment with two patients enrolled. No adverse events have been recorded. Subject accrual continues although the patient population from which to draw is small.



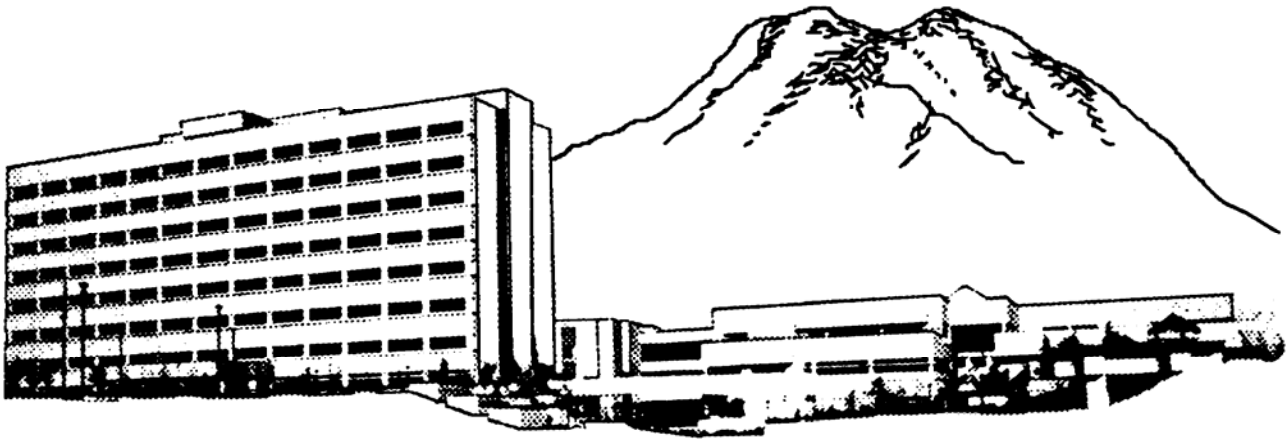
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205024	<b>Status:</b> Ongoing
<b>Title:</b> Computed Tomography of the Abdomen Following Appendectomy		
<b>Principal Investigator:</b> LTC John D. Statler, MC		
<b>Department:</b> Radiology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Joseph A. Ronsivalle, MC; CPT Andrew E. Fong, MC; CPT Brian C. Beldowicz, MC; CPT William T. Lewis, MC		
<b>Start - Completion:</b> 2/16/2005 - Feb 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/13/2005

**Study Objective:** To determine the computed tomography (CT) findings of patients who have recently undergone appendectomy.

**Technical Approach:** Adult male subjects will be recruited while in-hospital following their appendectomy. Relevant labs (serum creatinine) and history (contrast allergy) will be reviewed, and the subjects will be excluded from the study as indicated. Subjects meeting inclusion criteria and wishing to participate in the study will be assigned a random patient number. The PI will secure the code list. The subject will be given an appointment for CT scan of the abdomen on the same day as his follow-up appointment in the surgery clinic. Subjects will arrive at the Dept of Radiology, Computed Tomography section before their surgery clinic appointment. CT technologists will verify the subject's eligibility to undergo the exam. The subject will ingest approximately 1 1/2 liters of oral contrast. An intravenous line will be started. Following adequate time (approximately 2 1/2 hrs) to opacify the small bowel, CT of the abdomen and pelvis with oral and intravenous contrast will be obtained. The i.v. will be removed, and the subject will be discharged to the surgical clinic. Total participation time should take approximately 3 hours.

**Progress:** This protocol remains open to enrollment with sixteen subjects enrolled. No adverse events have occurred. One problem has been coaxing subjects to obtain final CT scan to complete the study; four subjects did not undergo the follow up CT scan.



## **Detail Summary Sheets**

Special Forces Group, Fort Lewis

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206106	<b>Status:</b> Ongoing
<b>Title:</b> 1st Special Forces Group (Airborne) Combat Trauma Management Procedures Training for Special Forces Medical Personnel		
<b>Principal Investigator:</b> COL Eric P. Wendt		
<b>Department:</b> Special Forces	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Lane A Hansen; Frank J. Newton		
<b>Start - Completion:</b> 7/13/2005 - Jul 2008	<b>Funding:</b> 1st Special Forces Group (Airborne)	<b>Periodic Review:</b> N/A

**Study Objective:** Trauma is the leading cause of death among American ages 1-44. The purpose of this training exercise is to teach critical trauma management and resuscitative tasks. This exercise emulates, in part, the instruction in the Special Forces Medical Sergeant's/Advanced Special Operations Combat Medic course. It is intended to teach lifesaving procedures under simulated tactical scenarios which are stressful, challenging and austere.

**Technical Approach:** Combat management training is conducted in a simulated battlefield on a multiply wounded patient. The student must accurately access the patient, resuscitate him, and then treat the wounds in a timely manner. The student will perform a preliminary physical examination of the animal subject and determine that the subject can safely tolerate the physiologic demands of general anesthesia, wounding and resuscitation. The animal is placed under general anesthesia using intravenous anesthetic agents. When the animal has reached the appropriate level of anesthesia, an instructor inflicts simulated battlefield injuries. The animal is transported to a Combat Trauma Management scenario for resuscitative procedures. The student is immediately summoned and begins an exercise comprised of primary and secondary assessments, resuscitation, wound treatment and casualty evacuation. The successful student will recognize life threatening conditions and initiate immediate and appropriate medical treatment. The protocol is also used to sustain medical skills of those who have already graduated from the JSOMTC or its predecessor, the "Med Lab." This specifically applies to the Special Forces Medical Sergeant's Advanced Non-Commissioned Officer's Course Combat Trauma Management Procedures Training or the Special Operations Forces Medical Skills Sustainment Program.

**Progress:** No goats have yet been utilized for this protocol.

### Detail Summary Sheet

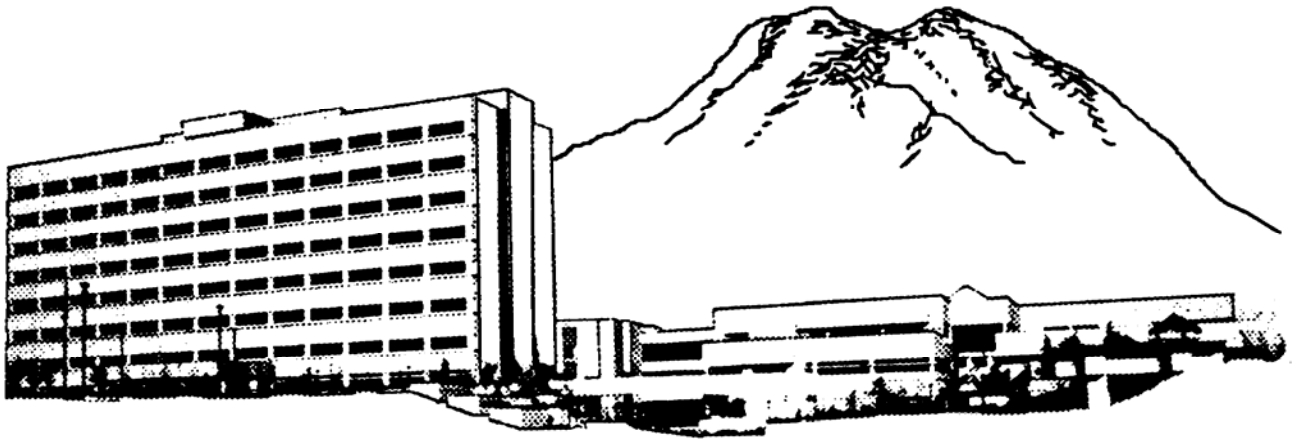
<b>Date:</b> 30 Sep 06	<b>Number:</b> 206018	<b>Status:</b> Ongoing
<b>Title:</b> 1st Special Forces Group (Airborne) Instructing Combat Trauma Management to Trainees		
<b>Principal Investigator:</b> COL Eric P. Wendt		
<b>Department:</b> Special Forces		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Lane A Hansen; Frank J. Newton		
<b>Start - Completion:</b> 7/13/2005 - Jul 2008	<b>Funding:</b> 1st Special Forces Group (Airborne)	<b>Periodic Review:</b> N/A

**Study Objective:** To allow SOMO instructors to train SOMNCOs in methods of teaching selected volunteers to perform lifesaving medical procedures and to recognize the indication for these procedures.

**Technical Approach:** CTM training is conducted in a simulated battlefield on a multiple wounded patient. The medic acting as Student-Trainer must teach accurate assessment and resuscitation of the patient. The student-Trainer must instruct the trainees in how to treat the wounds in a timely manner. The Student-Trainer will begin by demonstrating to the Instructor-Trainer how to perform a preliminary physical examination of the animal subject in order to determine whether the animal can safely tolerate the physiologic demands of general anesthesia, wounding, and resuscitation. The animal is then placed under general anesthesia by the Student-Trainer (under supervision of the Attending Veterinarian) using intravenous and/or inhalant anesthetic agents. When the animal has reached the appropriate level of anesthesia, the Student-Trainer inflicts simulated battlefield injuries. The animal is transported to a Combat Trauma Management scenario for resuscitative procedures.

The Trainees/Volunteers will immediately be summoned with the battlefield call of "MEDIC", "Corpsman" or a regionally appropriate foreign language equivalent title, and will then begin an exercise comprising primary and secondary assessments, resuscitation, wound treatment, and casualty evacuation. The Special Operations Medic acting as the Student-Trainer will be graded on how successfully he teaches, coaches and mentors the Volunteers in recognizing life-threatening conditions and in initiating immediate and appropriate medical treatment.

**Progress:** Fifteen animals were utilized to train 9 Trainers and 72 Students during FY06.



## Detail Summary Sheets

General Surgery Service, Department of  
Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206032	<b>Status:</b> Ongoing
<b>Title:</b> Colonic Ischemia Following Abdominal Aortic Aneurysm Repair-- Open vs. Endovascular Approaches		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Scott R. Steele, MC; LTC Matthew J. Martin, MC; MAJ Philip S. Mullenix, MC; LTC Benjamin W. Starnes, MC; COL (Ret) Charles A. Andersen, MD; COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 12/14/2005 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if there are any differences in colonic ischemia complications following abdominal aortic aneurysm repair using an open versus an endovascular approach and determine any peri-operative factors which may contribute to that difference.

**Technical Approach:** This is a retrospective review comparing a consecutive series of endovascular repairs for abdominal aortic aneurysms. A chart review of all cases of the endovascular approach will be performed and results compared to historical controls of the open approach. Open patients will be consecutive patients coming from the time period just preceding the startup of the endovascular approach. ORMA will be used to generate the patient names for each of the two methods to perform the chart review.

**Progress:** A review of just over 70 EVAR cases identified that only one colorectal complication occurred with those procedures. Data collection continues with all open cases. Investigators plan to seek collaboration with other military medical facilities and extend this protocol as a multisite study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206123	<b>Status:</b> Ongoing
<b>Title:</b> Renovascular Hypertension: A Retrospective Analysis of Renal Artery Stenting Outcomes		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; CPT Vance Y. Sohn, MC; COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 9/13/2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** 1. To establish the impact of renal artery stenting on patients hypertension control and on their renal function.  
2. To determine the natural history of patients that have not been treated with stenting of the renal arteries.

**Technical Approach:** To perform a retrospective review of inpatient and outpatient records for patients that were presented at a Multidisciplinary Renovascular Conference, which included nephrologists, interventional radiologists, and vascular surgeons. Patients with atherosclerotic renal artery disease are to be included between January 2001 and June 2006. Patients presented at this conference were referred by nephrologists for multiple medication hypertension, worsening renal function, or congestive heart failure. The multidisciplinary team evaluated each patient for potential renal artery stenting, and as a result there was a cohort of patients that were followed with medical management. Reasons patients were not offered stenting include: inadequate anti-hypertensive regimen, poor patient compliance, acute medical conditions, resistive indice  $>0.80$ , and lesions that were  $<70\%$  stenosis. A retrospective chart analysis will be performed of inpatient and outpatient up records. The patients that were not offered stenting will be used as a comparison against the population that underwent stenting. While not an adequate control since these patients were selected by the conference, they will provide a comparison for the natural history of worsening renovascular disease. Initial screening of the renal vascular bed is performed with duplex ultrasound criteria, and if the study was noncontributory, magnetic resonance angiography (MRA) or computed tomographic angiography (CTA) was performed as a confirmatory test.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee, effective 20 September 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203090	<b>Status:</b> Ongoing
<b>Title:</b> The Association Of Elevated C-Reactive Protein With Presence And Degree Of Carotid Stenosis		
<b>Principal Investigator:</b> CPT Zachary M. Arthurs, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Philip S. Mullenix, MC; COL (Ret) Charles A. Andersen, MD; Leslie B. Schoneman, PA-C; CPT Garth S. Herbert, MC; CPT Craig S. See, MC; LTC Benjamin W. Starnes, MC; CPT Katharine E. Wolcott, MC; CPT Daniel G. Cuadrado, MC; MAJ Allen D. Rubin, MC		
<b>Start - Completion:</b> 7/1/2003 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/28/2006

**Study Objective:** Evaluate the association between serum CRP levels and the presence and degree of carotid stenosis.

**Technical Approach:** This is a prospective observational concurrent cohort study evaluating the potential relationship between serum C-reactive protein levels and the presence and degree of carotid stenosis. It involves two study arms, a cohort with carotid stenosis, and one without, as defined by bilateral carotid duplex ultrasound. The study involves two phases. Phase I will (1) compare the measured initial CRP means between the two cohorts, and (2) correlate the amount of elevation of CRP with the measured degree of carotid stenosis. Phase II is a longitudinal study designed to stratify increased risk of progression of carotid disease or adverse neurologic outcomes using odds ratios generated from measured CRP quartile means.

**Progress:** This protocol closed to enrollment with 361 subjects enrolled. Of that number 72 will complete their three-year involvement by December 2006 and the protocol will continue until the remaining subjects reach their three-year study participation.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203107	<b>Status:</b> Completed
<b>Title:</b> A Multicenter, Open-Label, Randomized Study To Compare The Safety And Efficacy Of Once Daily Levofloxacin Along With Once Daily Metronidazole Versus Piperacillin / Tazobactam In The Treatment Of Complicated Appendicitis, Protocol CAPSS-151		
<b>Principal Investigator:</b> COL Kenneth S. Azarow, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Alec C. Beekley, MC; MAJ James A. Sebesta, MC; CPT Amy L. Young, DO; LTC Robert M. Rush, MC; Margaret I. Voelker, RN, CRC; CPT Troy P. Houseworth, MC; CPT Rebecca M. McGuigan, MC; CPT Neil R. Stockmaster, MC; CPT Craig S. See, MC; CPT James C. Nunley, MC		
<b>Start - Completion:</b> 11/18/2003 - Oct 2006	<b>Funding:</b> Ortho-McNeil Pharmaceutical via Henry M. Jackson Foundation	<b>Periodic Review:</b> 8/10/2006
<p><b>Study Objective:</b> Primary: To determine the safety and efficacy of the treatment regimen containing levofloxacin and metronidazole compared to the regimen of Piperacillin/Tazobactam in the treatment of complicated appendicitis. Secondary Objectives: To assess clinical response at Post-therapy visit among microbiologically evaluable patients; to assess clinical response at post study phone contact among clinically and microbiologically evaluable patients; To assess microbiologic response at Post-therapy visit by patient and by pathogen(s) isolated at study entry among microbiologically evaluable patients; to compare total costs associated with care (average length of hospital stay, cost of drugs, administration costs, time to oral switch, and duration of treatment) for each treatment group.</p> <p><b>Technical Approach:</b> This is a multicenter, open-label, randomized study comparing two treatments for complicated appendicitis in male and female patients 18 years or older. Approximately 1500 subjects will be enrolled in the trial for the goal of 420 evaluable patients. At MAMC, 10-20 subjects may be enrolled over 2-3 years. Patients suspected of having complicated appendicitis and requiring surgery will be screened for enrollment by study investigators of the MAMC General Surgery Service. Patients meeting eligibility criteria will be randomized in 1:1 ratio to two treatment groups. The first antibiotic regimen dose is given prior to surgery. Group 1 will receive the drug combination under study, levofloxacin 750 mg, IV, every 24 hours followed by metronidazole 1500 mg, IV, every 24 hours. After at least 48 hours of IV administration, patients may be switched to oral levofloxacin 750 mg every 24 hours and metronidazole 1500 mg by mouth every 24 hours. The oral antibiotics will be continued for a total of 4 - 14 days of therapy. Group 2 will receive the comparator regimen, Piperacillin/Tazobactam 3.375 grams, IV, every 6 hours. The first dose is given before surgery. Patients may be switched after 48 hours of IV therapy to oral amoxicillin/clavulanate 875/125 every 12 hours for a total of 4 - 14 days.</p> <p>Patients who are found at surgery to have appendicitis complicated by rupture and intra-abdominal/peritoneal infection will be continued in the study. Fluids for culture and sensitivity testing will be obtained intraoperatively and sent to MAMC clinical laboratory and the study central laboratory. Patients who do not have complicated appendicitis confirmed will be discontinued from the study to receive interventions per clinical standards.</p> <p>Patients will return after hospital discharge for a follow-up assessment at the end of treatment and a telephone contact will be done for data collection at 30 days after end of treatment. Assessments performed during hospitalization and at follow up include evaluation of clinical symptoms and signs, adverse events, vital signs, concomitant medications, hematology and serum chemistry assays. Patients with baseline positive blood cultures will receive appropriate follow up</p>		

blood cultures during and after therapy. Study design includes procedures for unscheduled follow up in the case of postoperative wound infection or an intra-abdominal abscess. A modified intent to treat population will be utilized including all randomized patients who receive at least one dose of study drug and are found to have complicated appendicitis. Clinical efficacy will be evaluated by clinical and microbiological response. Hospital resource use will be evaluated by length of stay and length of antibiotic treatment. Safety analysis will examine incidence, severity, types of adverse events, changes in physical findings and abnormalities in vital signs and laboratory values. An interim analysis will be performed.

**Progress:** This protocol completed all study related activity during FY05 and was reported completed at MAMC in September 2006, with thirteen patients consented/completed study visits and four patients documented as lost to follow-up.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204013	<b>Status:</b> Completed
<b>Title:</b> Abdominal Wall Defects: Does the Intraabdominal Pressure Affect Outcome?		
<b>Principal Investigator:</b> COL Kenneth S. Azarow, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Rebecca M. McGuigan, MC		
<b>Start - Completion:</b> 11/12/2003 - Nov 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11/22/2005

**Study Objective:** To retrospectively analyze neonates with abdominal wall defects at Madigan since 1997 in order to determine whether splanchnic perfusion pressure affects and/or is predictive patient outcome.

**Technical Approach:** This study is a retrospective chart review of all patients treated at Madigan Army Medical Center with congenital abdominal wall defects diagnosed at birth. The effect of intragastric and intraabdominal pressure and "splanchnic perfusion pressure" on the incidence of complications and overall outcome will be analyzed.

**Progress:** This protocol was reported completed during FY06. A paper was published in Journal of Pediatric Surgery adding MAMC results to those of Children's Hospital Seattle and Children's Hospital of Illinois, Peoria. "McGuigan, Mullenix, Vegunta, Peal, Sawin, and Azarow. Splanchnic Perfusion Pressure: a better predictor of safe primary closure than intraabdominal pressure in neonatal gastroschisis." J Pediatr Surg 2006. 41: 901-904.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204058	<b>Status:</b> Ongoing
<b>Title:</b> Advanced/Combat Trauma Management Training Using Animal Models (Domestic Goat/Capra hircus, Pig/Sus scrofa)		
<b>Principal Investigator:</b> MAJ Alec C. Beekley, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ James A. Sebesta, MC; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 3/10/2004 - Mar 2007	<b>Funding:</b> Units via MOU	<b>Periodic Review:</b> 3/8/2006

**Study Objective:** This protocol is intended to facilitate advanced and combat trauma management training of federally affiliated (e.g. DoD AC/RC, VA) physicians and ancillary medical personnel (e.g. nurse, physician's assistant, medic, medical/surgical technician, etc.).

**Technical Approach:** The protocol supports three levels of trauma management training, as follows: 1) Combat Relevant Trauma Management training for surgeons (CTM-S), focusing on preservation of life, limb, critical organ function, and casualty stabilization prior to medical evacuation for definitive care. 2) Combat-relevant Trauma Management training for physicians (CTM-P), focusing on preservation of life, limb, critical organ function, and casualty stabilization prior to medical evacuation for definitive care. 3) Combat-relevant Trauma Management training for ancillary medical personnel (CTM-NP), focusing on "hands-on" training of mission/duty-related trauma intervention procedures. Training associated with this protocol will utilize both inanimate (e.g. mannequin, cadaver, Simman, etc.) and live, anesthetized animal models. Whenever feasible, inanimate models will be used in place of live animals. Animal species used for this protocol will include goat and swine. The number of animals required is based on deployment of troops: Swine - Three to five personnel per animal, estimated that not more than 50 would be used per year. Goat - Three to five personnel per animal estimated that not more than 250 would be used per year.

**Progress:** Twelve labs were held during FY 06, providing predeployment combat casualty training for 194 medics and 28 3rd year Madigan residents, using 46 animal models. Protocol will continue with labs planned for training 200 medics and 30 3rd year Madigan residents in FY 2007.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205075	<b>Status:</b> Ongoing
<b>Title:</b> Operation Iraqi Freedom Combat Trauma Database from the 31st Combat Support Hospital, Baghdad, Iraq		
<b>Principal Investigator:</b> MAJ Alec C. Beekley, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ James A. Sebesta, MC; LTC Tommy A. Brown, MC; COL (Ret) Charles A. Andersen, MD; COL Kenneth S. Azarow, MC; MAJ Philip S. Mullenix, MC; CPT Zachary M. Arthurs, MC; CPT Randy J. Kjorstad, MC; CPT Troy P. Houseworth, MC; CPT Rebecca M. McGuigan, MC; CPT Daniel G. Cuadrado, MC		
<b>Start - Completion:</b> 5/6/2005 - Jan 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** To retrospectively review the recorded combat trauma, burn, pediatric, vascular, elective, and humanitarian surgical activities collected at the 31st Combat Support Hospital, Baghdad, Iraq between 1 Jan 04 and 31 Dec 04 that was recorded in an existing, secure, and confidential database for purposes of (1) continuous quality analysis/improvement of military surgical care in combat and (2) academic publication and presentation.

**Technical Approach:** Retrospective database (spreadsheet) review. Specific study questions (spreadsheet queries) will be submitted as specific addendums. Examples of typical study questions of interest might include (descriptive data analysis of existing spreadsheet only): Incidence of military admissions compared to civilian admissions at a large CSH. Primary and secondary surgical procedures performed compared between various patient subsets. Percentage of patients requiring ICU admissions compared between various patient subsets. Mortality rate of patients compared between various patient subsets. Length of ICU and Hospital stay compared between various patient subsets. Admission laboratory data to include vitals, Glasgow coma score, complete blood count, arterial blood gas with base deficit, and blood products administered. Distribution of primary and secondary cause of injury compared between various patient subsets. Incidence of damage control operations and operative times compared between various patient subsets. Injury severity scores compared between various patient subsets. Cause of death compared between various patient subsets. Proportion of patients that received level one or level two care as compared between various patient subsets.

Procedures: Dr. Beekley (PI) and Dr. Beekley alone will create code list for patient name/SSN. He will then permanently delete PHI (name/SSN/PHI) field columns from Excel spreadsheet and replace with code list number. Then he will permanently destroy all records of name/SSN/PHI leaving only the code list number. Even the PI will not have PHI after that point, and none of the AI's will ever see PHI. Decide on a specific study question of interest for database query. Submit addendum to this protocol to MAMC IRB with specific question and variables to be analyzed. Cut and paste pertinent study data from secure de-identified computerized Excel spreadsheet file into new spreadsheet specific to that problem (delete irrelevant fields, calculate new variables from existing data). Maintain the new spreadsheet in same secure, de-identified manner using existing code list system.

Analyze data. Due to the nature of the database and fields available, these statistical analyses employed will be straightforward, descriptive, and observational in nature, in general designed to compare various subset cohorts identified within the total data set. Report and present data in entirely de-identified fashion (no names, patient numbers, patient specific data or identifiable injury pattern, etc - typical chart review reporting). Destroy code list specific to that study question and destroy all hard copies if any.

**Progress:** Institute of Surgical Research recently (as of mid-October 2006) completed accurate Injury Severity Scores for the patients in the 31st CSH database. Analysis of this data is ongoing. Planned comparison to outcomes from Trisat database in San Antonio is expected to start in next 1-2 months.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204106	<b>Status:</b> Completed
<b>Title:</b> A Multicenter, Double-blind, Randomized, Phase 3 Study to Compare the Safety and Efficacy of Intravenous Doripenem with that of Meropenem in Complicated Intra-abdominal Infections		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC; CPT Farah A. Husain, MC; CPT Garth S. Herbert, MC; CPT Kathleen M. Goings, MC; MAJ Scott R. Steele, MC; MAJ Philip S. Mullenix, MC; CPT Garth S. Herbert, MC		
<b>Start - Completion:</b> 11/5/2004 - Dec 2005	<b>Funding:</b> Peninsula Pharmaceuticals, Inc via The Geneva Foundation	<b>Periodic Review:</b> 7/27/2005

**Study Objective:** Primary objective: to compare the clinical response of Doripenem vs. Meropenem in hospitalized subjects with complicated intra-abdominal infections (cIAI) at the test-of-cure visit (TOC). The TOC visit is the late follow-up visit (4 to 6 weeks after the completion of therapy). Secondary objectives: (1) to compare the microbiological response of doripenem vs. Meropenem at the test-of-cure visit (4 to 6 weeks post-treatment), (2) to compare the clinical response of doripenem vs. Meropenem at the early follow-up visit (1 to 2 weeks post-treatment), (3) to compare the microbiological response of doripenem vs. Meropenem at the early follow-up visit (1 to 2 weeks post treatment), and (4) to compare the safety of IV doripenem with that of Meropenem.

**Technical Approach:** Subjects will be stratified before randomization based on primary sites of infection complicated appendicitis versus diagnosis of other sites of intra-abdominal infections and severity of illness (APACHE II score less than or equal to 10 or more than 10. Subjects will be assigned to study drug regimen using a computerized randomization to minimize bias. Except for the responsible study site pharmacist or designee, all study participants will be blinded to the IV dosing regimen of all subjects. Aerobic and anaerobic specimens for culture will be collected at the time of the initial procedure (within 24 hours of enrollment). Aerobic specimens will be cultured and quantified in the local laboratory. The isolate(s) will be sent to a central, reference laboratory for validation of identification and susceptibility testing. All anaerobic specimens of infected fluid or tissue will be sent in transport medium directly to a central, reference laboratory for anaerobic isolation, identification, and susceptibility testing.

After at least 6 doses (approximately 48 hours) of IV study drug therapy administered while subjects are hospitalized, subjects may be discharged if arrangements are made for continued IV administration of study drug and the collection of all required study assessments. Subjects may be switched to oral amoxicillin/clavulanate tablets (875mg / 125mg twice daily) after 9 or more doses of IV study drug therapy if all of the following criteria are met: (1) Body temperature and WBC count are decreasing compared to Day 1 pre-dose. (2) Signs and/or symptoms of cIAI are absent or improved compared to Day 1 pre-dose and (3) Bowel function has returned. There should be at least 8 hours between the last dose of IV study drug and first dose of oral amoxicillin/clavulanate. After randomization, patients will receive Doripenem injection 500 mg 60-minute IV infusions q 8 hours or Meropenem 1 gm by IV bolus over 3-5 minutes q 8 hours. Addition of open-label vancomycin is permitted if Enterococcus or methicillin-resistant Staphylococcus aureus is one of the pathogens isolated. This study will last approximately 6 to 8 weeks. Screening may occur up to 24 hours prior to the infusion of the first dose of study drug. The total days of IV and oral study drug therapy will be 5-14 days. An early follow-up visit will be conducted 7-14 days after the final dose of study drug is administered. The TOC visit will be 28-42 days (4-6 weeks) after the final dose of study drug.

Clinical outcome assessment will be made at the early follow-up visit and at the TOC visit. Clinical response will be classified as cure, failure, or indeterminate based on clinical outcome. A favorable clinical response is "cure". Once a subject has an "unfavorable" response at any clinical assessment, the subject will be counted as having an "unfavorable" response at all subsequent time points.

**Progress:** This protocol was reported completed in June 2006, with six subjects enrolled; four completed, two dropped from study, and two internal serious adverse events reported.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206015	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective Randomized Study Comparing Sentinel Lymph Node (SLN) Evaluation with Standard Pathological Evaluation for the Staging of Colon Carcinoma		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Gregory P. Fitzharris, MC; MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC; LTC Robert M. Rush, MC		
<b>Start - Completion:</b> 6/9/2006 - Oct 2010	<b>Funding:</b> DCI	<b>Periodic Review:</b> 11/21/2006

**Study Objective:** The objective of this trial is to define the rate of upstaging of colon carcinoma lymph node metastasis with sentinel lymph node (SLN) mapping.

**Technical Approach:** Male and female military healthcare beneficiaries over the age of 18 years presenting at the General Surgery Clinic with the diagnosis of biopsy-proven, primary, non-metastatic (Clinical Stage I,II or III) colon carcinoma will be enrolled. Subjects with colonic masses clinically consistent with colon cancer and eventually confirmed by pathology, will also be enrolled. A total of 150 patients will be enrolled; up to 20 patients per year are expected to be enrolled at MAMC. A complete history and physical examination including demographic data, co-morbid conditions, past surgical history, clinical tumor staging, American Society of Anesthesiologists classification, height and weight will be performed within one month before surgery. Pre-operative evaluation will consist of complete blood count (CBC), coagulation profile (PT/PTT), screening profile including: electrolytes, blood urea nitrogen, creatinine, pulmonary function testing, chest radiography and electrocardiogram (at the discretion of the attending surgeon). Pre-operative clinical staging will be conducted according to MAMC current standard of care and will include colonoscopy and serum carcinoembryonic antigen (CEA).

Subjects randomized to the standard histopathology arm will undergo a standard surgical resection of the colon cancer. The entire surgical specimen (colon and mesentery) will be sent to the pathologist for standard histopathological evaluation and staging of the cancer using conventional paraffin embedding, sectioning and hematoxylin and eosin staining (H&E) and microscopy. Subjects randomized to the SLN arm of the trial will undergo standard surgical resection of the colon cancer including the normal wedge of mesentery containing the draining lymphatics. Immediately following resection the surgical specimen will be stained. The investigator will dissect all blue nodes from the mesentery and submit them to pathology as separately labeled specimens (SLNs). The remaining resected colon with attached mesentery will then be sent fixed in formalin for standard histopathological evaluation of non-SLNs, as per standard of care protocol. The SLN pathology results will be made available to both the subject and the subject's physician. Subject participation will conclude with the surgical procedure. No follow-up is required for this clinical trial.

**Progress:** This protocol remains open to patient entry, with two patients enrolled during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 205074	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Double-Blind Study of GT267-004 Versus Vancomycin, and GT267-004 Versus Metronidazole, in Patients with C.Difficile-Associated Diarrhea; Protocol GD3-170-301			
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC			
<b>Department:</b> Surgery/General Surgery			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC; MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC; Margaret I. Voelker, RN, CRC			
<b>Start - Completion:</b> 8/10/2005 - Jun 2007	<b>Funding:</b> Genzyme Corporation via Henry M. Jackson Foundation		<b>Periodic Review:</b> 4/25/2006

**Study Objective:** (1) To compare the safety tolerability of GT267-004 versus vancomycin, and GT267-004 versus metronidazole, inpatients with Clostridium difficile-associated diarrhea (CDAD). (2) To compare the effect of GT267-004 versus vancomycin, and GT267-004 versus vancomycin, and GT267-004 versus metronidazole, on the resolution of CDAD. (3) To compare the effect of GT267-004 versus vancomycin, and GT267-004 versus metronidazole, on the rate CDAD recurrence during the follow-up period. (4) To compare the safety, tolerability and efficacy of vancomycin versus metronidazole for resolution of CDAD and recurrence rates.

**Technical Approach:** This is a Phase III, double-blind study to compare the safety and efficacy of GT267-004 versus Vancomycin and GT267-004 versus Metronidazole for the treatment of clostridium difficile-associated diarrhea (CDAD). The study consists of a two week treatment period, during which patients will receive GT267-004, Vancomycin or metronidazole per randomization. The treatment period is followed by a 4 week follow-up period. The total study duration is 6 weeks. Patients randomized to the vancomycin dose group will receive a 10 day course given in combination with a 14 day course of GT267-004 placebo. Patients randomized to the metronidazole dose group will be given a 10 day course with a 14 day course of GT267-004 placebo. Patients randomized to the GT267-004 dose group will be given 14 days of in combination with 10 days of vancomycin or metronidazole placebo. During treatment, stool counts and consistency will be monitored daily by the study staff, either in person for inpatients or by phone for outpatients. Lab samples for serum potassium will be collected on days 4, 8 and 12 (+ 2 days). A complete exam with safety labs will be collected on Days 8 and 15. Recurrence rates will be followed for 4 additional weeks up to week 6 and will follow procedures outlined in section 12.6 of the protocol pages 28-29. Non-responders will have study treatment discontinued and will begin c-difficile treatment at needed.

**Progress:** A study site close out visit was conducted in September 2006. A total of 9 patients were screened for this protocol; only two were consented, randomized and enrolled. One subject completed the entire course of study treatment and follow-up. The other subject withdrew participation due to a serious adverse event, dehydration, which the PI deemed as anticipated for a person diagnosed with C.Difficile-associated diarrhea.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205096	<b>Status:</b> Completed
<b>Title:</b> ACOSOG Z4031, Use of Proteomic Analysis of Serum Samples for Detection of Non-Small Cell Lung Cancer		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Gregory P. Fitzharris, MC; MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC; LTC Robert M. Rush, MC		
<b>Start - Completion:</b> 3/3/2006 - Jul 2010	<b>Funding:</b> ACOSOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To determine prospectively whether the serum proteomic profile can predict the presence of primary NSCLC in patients with suspicious lung lesions who are candidates for lung resection. (2) To correlate the serum proteomic profile with pathologic nodal status and histopathologic features of primary lung cancer in patients with NSCLC undergoing lung resection. (3) To correlate the initial serum proteomic profile with overall and cancer-specific survival in patients with NSCLC undergoing lung resection. (4) To correlate the follow-up serum proteomic profile with overall and cancer-specific survival in patients with NSCLC undergoing lung resection. (5) To correlate changes in the proteomic profile (pre-operative to post-operative) with overall and cancer-specific survival in patients with NSCLC undergoing lung resection. (6) To acquire biospecimens prospectively and determine if novel molecular strategies can predict the presence of lung cancer and/or the biologic behavior of an individual cancer.

**Technical Approach:** This study will collect pre and post surgical serum samples on about 1200 patients having surgical resection for suspected non-small cell carcinoma. Patients who are found to have a malignant tumor will also have tissue samples submitted. Protein profiling will be done on samples to search for diagnostic and prognostic indicators. Patients who are eligible to participate will have data collected on in the form of history and physical exam, radiologic reports, and operative reports. Patients found to have benign tumors will be followed yearly for 2 years for survival data. Patients found to have malignant tumors will be followed annually for 5 years for survival data. This study is to prospectively determine whether the serum proteomic profile can predict the presence of primary lung cancer in patients with suspicious lung lesions who plan to undergo a lung resection for diagnosis or treatment. For statistical modeling, the estimated number of patients needed is: 300 patients with benign diagnosis, 350 patients with adenocarcinoma, 200 patients with squamous cell carcinoma, and 150 patients with other types of malignant tumors. Patients with mixed histology will be assigned to the group of the predominant cell type. In order to have at least 300 patients with a benign pathologic diagnosis, a sample size recalculation will be conducted when about 800 patients are entered into the study, to increase the sample size by up to 20%. With an expected annual accrual of 500 patients, it will take approximately 2 years for total accrual. The patients will be followed for an additional 2 or 5 years after the completion of accrual for the survival endpoint, depending on final diagnosis.

**Progress:** Accrual goals were met as of 17 April 2006, and the protocol was reported completed with no subjects enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206101	<b>Status:</b> Ongoing
<b>Title:</b> ACOSOG Z6041: A Phase II Trial of Neoadjuvant Chemoradiation and Local Excision for uT2uN0 Rectal Cancer		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC William B. Reece, MC; MAJ Joseph P. Brooks, MC; MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 10/10/2006 - Aug 2010	<b>Funding:</b> ACOSOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Objectives: To determine the rate of disease-free survival at 3 years in ultrasound-staged uT2uN0 rectal cancer patients treated with chemoradiation (CRT) followed by local excision (LE). To determine the rate of respectability with negative margins, procedure-specific morbidity and mortality, and quality of life in ultrasound-staged Ut2uN0 rectal cancer treated with neoadjuvant CRT followed by LE. To determine the feasibility of using molecular studies to assess surgical resection margins and tumor response to neoadjuvant CRT.

**Technical Approach:** This is a Phase II study of preoperative chemoradiation in patients with uT2uN0 rectal cancer. Patients will be identified and consented in the Surgical Oncology department. Prior to registration they will have a physical exam; lab work, scans and quality of life questionnaires (QOL). Eligible patients will be registered and begin treatment. Prior to chemoradiation patients will have biopsy samples collected and tumor tattooing to mark tumor measurement. Chemotherapy will be given as oral capecitabine on days 1-14 and 22-28, and IV oxaliplatin on days 1, 8, 22, and 29. Radiation therapy will be given concurrently according to standard therapy, five days a week, for weeks 1 through 5. During chemoradiation, patients will be followed with weekly exams, adverse advent assessment and lab tests. At week 12, patients will have local excision of remaining tumor, including collection of tissue specimens for correlative studies, and measurement of tattoo marks to mark response to treatment. Follow up will take place at Month 4 and every 4 months through Year 3. Patients will be followed every 6 months through Year 5. Follow-up procedures will include proctoscopy and CEA, endorectal ultrasound, and QOL.

**Progress:** This protocol remains open to patient entry, with no patients enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205098	<b>Status:</b> Terminated
<b>Title:</b> ACOSOG Z9031, A Phase III Randomized Study of Preoperative Radiation Plus Surgery Versus Surgery Alone for Patients with Retroperitoneal Sarcomas (RPS)		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC William B. Reece, MC; MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC; LTC Robert M. Rush, MC; LTC John B. Halligan, MC		
<b>Start - Completion:</b> 1/9/2006 - Jul 2010	<b>Funding:</b> ACOSOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate whether preoperative radiotherapy of 45.0-50.4 Gy plus surgery improves the PFS compared to surgery alone in patients with primary RPS. Secondary Objectives: (1) To assess the toxicity and complications associated with preoperative radiotherapy and surgery. (2) To assess whether preoperative radiation increases the rates of microscopically complete surgical resection (R0). (3) To assess whether preoperative radiation increases the overall survival rate of patients with RPS.

**Technical Approach:** Up to 370 patients with primary RPS will be enrolled to this study, with approximately 2 patients per year enrolled at MAMC. Patients in the surgical arm will have a history and physical, surgical consult, scans including chest x-ray, CT, and IV pyelogram, and lab tests including CBC, Chemistry, LFT's and urine or serum pregnancy test for women of child bearing potential. Post surgery, patients will be followed with physical exam, chest x-ray and CT scans at Month 4, every 6 months afterwards until Year 5, then annually until 10 years or death, whichever comes first. Patients on the radiation therapy arm will have the same procedures, and in addition will receive radiation therapy once a day, 5 days a week, for five and a half weeks. Patients will also be offered participation in the specimen correlative study. Blood samples will be collected prior to radiation therapy, prior to surgery, post surgery, at yearly follow-up and at recurrence. Tissue samples will be taken from tumor already removed at time of surgery.

The primary analysis will be by randomized arm (intent-to-treat). PFS and overall survival (OS) data will be analyzed using the log-rank test and Cox regression. Toxicity (grade 2 or lower vs. 3 or higher), complications and resectability (complete resection vs. others) data will be analyzed using the chi-squared test and logistic regression method. The multivariate data analyses will compare the two arms adjusting for the stratification factors and some additional covariates such as age (65 years old or younger vs. 65+ years), macroscopically complete resection (yes vs. no), microscopic surgical margin status, and anatomic location (pelvic epicenter vs. non-pelvic). For a direct comparison of our results with those from other studies, subset analyses will be conducted for: (1) the subset of patients that undergo macroscopically complete tumor resection, and (2) the subset of patients that undergo macroscopically incomplete resection or no surgery.

**Progress:** This protocol received final approval on 9 January 2006; however, the ACOSOG terminated the study due to lack of accrual in March 2006. No subjects enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205097	<b>Status:</b> Terminated
<b>Title:</b> Biological Relevance of Sentinel Lymph Node (SLN) Micrometastasis in Patients With Colon Carcinoma		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Gregory P. Fitzharris, MC; MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC; LTC Robert M. Rush, MC		
<b>Start - Completion:</b> Never approved	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective of this study is to determine the prognostic significance of molecular staging of colon carcinoma on the basis of sentinel lymph node mapping and analysis.

**Technical Approach:** Up to 200 male or female military health care beneficiaries over the age of 18 with a diagnosis of biopsy-proven, primary, non-metastatic (Clinical Stage I-III) colon carcinoma will be enrolled in this study over a 3-4 year period. Subjects with colonic masses clinically consistent with colon cancer will also be enrolled. Those subjects with masses clinically consistent with cancer will be dropped if a diagnosis of colon cancer is not confirmed by pathology. Specimen collection and pathologic processing will be conducted as described in the master protocol. Patients will be followed for signs and symptoms of disease recurrence post-operatively according to standard of care that consists of history and physical examination and serum CEA every three months for 2 years, then every 6 months for two years then annually. A CXR will be performed annually following primary colon resection. A colonoscopy will be performed on year and three years post-operatively. If the 3 year post-op colonoscopy is normal, then follow-up will be performed every 5 years thereafter.

**Progress:** This protocol received initial IRB approval with stipulations, 28 Jun 05; however, the PI terminated the study prior to final approval in October 2006, as the Department of Pathology could not support the study.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203077	<b>Status:</b> Expired
<b>Title:</b> Comparative Medical/Surgical Research and Development (Limited)		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 4/16/2003 - Apr 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7/12/2006

**Study Objective:** 1) To facilitate preliminary investigations of proposed animal research models and pilot studies, as well as the practice of newly described surgical procedures on animals prior to use in human patients in an effort to refine and reduce the sacrifice of animals and enhance the quality and effectiveness of medical/surgical patient services at MAMC. 2) To provide uniform standards and assurances of proper animal care and use in the conduct of limited animal model development, pilot studies and surgical advancement training proposed by MAMC-affiliated medical staff.

This protocol is designed to facilitate preliminary investigative medical and surgical research and development as described below: a) Development or refinement of animal models for medical/surgical research or training. b) Limited pilot studies (animal) that are preliminary to more extensive research proposals. c) Practice of newly described surgical procedures, animal models prior to utilization in the MAMC human surgical patient population.

**Technical Approach:** The details of experimental design and general procedures will be provided in each addendum to this protocol. The MAMC/DCI veterinarian (PI) will be consulted in the development of all addenda to this protocol.

1. Proposed animal model development/refinement will be based on previously described animal models that are considered to be flawed, recognized similarities in comparative physiological/anatomical characteristics of particular animal species and humans or similarities in disease processes. Pilot studies will likewise reference applicable similarities in comparative physiological/anatomical features between proposed animal models and humans as related to the investigative question posed in the study. Practice of newly described surgical procedures will be conducted on animal species possessing the most comparable organ systems of interest, then compared to human anatomy and physiology.

2. Where applicable, animals will receive species-specific pre-anesthetic medication, anesthesia and post surgical analgesia (as applicable ) as described in Section V.C.2.b., 3.a. and 7.b (1) of Technical Methods. Requirements for pre, intra and/or post-operative biosample (e.g. blood, urine, etc) collection or diagnostic imaging ( e.g. radiography ultrasonography, etc.) will be described in Section V.C.3.b, and e. of Technical Methods in each procedure-specific addendum.

3. Procedural descriptions and post-operative care instructions will be provided in Sections V.C.2.a and b. of Technical Methods and V.D.1. and 2. of Veterinary Care in each addendum. Methods of euthanasia and study endpoints will be described in Section V.C.3.5. and 6. of the Technical Methods in each addendum.

**Progress:** One amendment was submitted to do a pilot study, using pigs, to develop a urinary diversion technique to teach urology residents during laparoscopic training. Two pigs were used successfully and this technique will be incorporated into future urology laparoscopic training labs.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206110	<b>Status:</b> Ongoing
<b>Title:</b> Comparative Medical/Surgical Research and Development (Limited)		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; MAJ James A. Sebesta, MC; CPT Matthew J. Eckert, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 7/12/2006 - Jul 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To facilitate preliminary investigations of proposed animal research models and pilot studies, as well as the practice of newly described surgical procedures on animals prior to use in human patients in an effort to refine and reduce the sacrifice of animals and enhance the quality and effectiveness of medical/surgical patient services at MAMC.

To provide uniform standards and assurances of proper animal care and use in the conduct of limited animal model development, pilot studies and surgical advancement training proposed by MAMC-affiliated medical staff.

This protocol is designed to facilitate preliminary investigative medical and surgical research and development as described below: a) Development or refinement of animal models for medical/surgical research or training. b) Limited pilot studies (animal) that are preliminary to more extensive research proposals. c) Practice of newly described surgical procedures, animal models prior to utilization in the MAMC human surgical patient population.

**Technical Approach:** The details of experimental design and general procedures will be provided in each addendum to this protocol. The MAMC/DCI veterinarian (PI) will be consulted in the development of all addenda to this protocol.

1. Proposed animal model development/refinement will be based on previously described animal models that are considered to be flawed, recognized similarities in comparative physiological/anatomical characteristics of particular animal species and humans or similarities in disease processes. Pilot studies will likewise reference applicable similarities in comparative physiological/anatomical features between proposed animal models and humans as related to the investigative question posed in the study. Practice of newly described surgical procedures will be conducted on animal species possessing the most comparable organ systems of interest, then compared to human anatomy and physiology.
2. Where applicable, animals will receive species-specific pre-anesthetic medication, anesthesia and post surgical analgesia (as applicable) as described in Section V.C.2.b., 3.a. and 7.b (1) of Technical Methods. Requirements for pre, intra and/or post-operative bio-sample (e.g. blood, urine, etc) collection or diagnostic imaging (e.g. radiography ultrasonography, etc.) will be described in Section V.C.3.b, and e. of Technical Methods in each procedure-specific addendum.
3. Procedural descriptions and post-operative care instructions will be provided in Sections V.C.2.a and b. of Technical Methods and V.D.1. and 2. of Veterinary Care in each addendum. Methods of euthanasia and study endpoints will be described in Section V.C.3.5. and 6. of the Technical Methods in each addendum.



**Progress:** One amendment was approved for the prior protocol of the same title and carried into this new protocol. The amendment, using four pigs for a pilot study to establish a hemorrhage model, it was unsuccessful. No further work will be done, this protocol will be terminated in Nov 2006.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205112	<b>Status:</b> Ongoing
<b>Title:</b> RTOG 0412 / SWOG S0332, Phase III Randomized Trial of Preoperative Chemotherapy Versus Preoperative Concurrent Chemotherapy and Thoracic Radiotherapy Followed By Surgical Resection and Consolidation Chemotherapy in Favorable Prognosis Patients with Stage IIIA (N2) Non-Small Cell Lung Cancer		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC; LTC John B. Halligan, MC; LTC William B. Reece, MC; MAJ Angela G. Mysliwiec, MC; MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC		
<b>Start - Completion:</b> 12/15/2005 - Aug 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> 7/10/2006

**Study Objective:** (1) To prove that the preoperative regimen, consisting of thoracic radiation therapy given concurrently with chemotherapy followed by surgical resection, results in a significant improvement in overall survival compared to preoperative chemotherapy alone followed by surgical resection, with both arms receiving postoperative consolidation therapy (2) comparison of progression-free survival, median survival time, and toxicity and response rates (clinical and pathologic) in both treatment arms (3) evaluate the correlation of the pCR with the disease-free and overall survival (4) to investigate the association of DNA damage repair genes (ERCC1 and XRCC1), microtubule- related proteins (TUBB-III and MAP4), and shed tumor DNA with patient responses and outcomes to the platinum/taxane/radiation therapy in this trial (5) to employ MALDI-TOF proteomic analysis of tumor and serum to identify protein profiles associated with response to therapy and prognosis (6) to evaluate the role of FDG-PET post-therapy in predicting long-term outcome, as well as pathological response both in the tumor and in the mediastinal lymph nodes (7) to assess patient-reported functional status as an endpoint with potentially relevant differences between the two arms and (8) to determine the impact of co-morbid conditions on survival.

**Technical Approach:** This study is a randomized trial of preoperative chemotherapy versus concurrent chemoradiation followed by resection and consolidation in patients with Stage IIIA NSCLC. Up to 547 subjects will be enrolled in this study over a period of approximately four years with up to 6 subjects a year expected to enroll at MAMC. Patients in the chemotherapy arm will receive induction therapy with CDDP at 75 mg/m<sup>2</sup> on Days 1 and 22. Patients on the chemoradiation arm will receive CDDP at 50 mg/m<sup>2</sup> on days 1, 8, 22, and 29, with concurrent radiation therapy delivered 5 days a week for a total of 50.4 Gy. Both groups will be reevaluated 3 to 5 weeks after induction, and then continue to resection if there is no progression of disease. Patients in both arms will receive consolidation chemotherapy 4 to 6 weeks after surgery. Consolidation will consist of Docetaxel, 75 mg/m<sup>2</sup> on Days 1, 22 and 43, with growth factor support 24 hours after each chemo dose. Randomization to either arm will be stratified based on extent of nodal involvement, nodal micro-metastases, and T stage. Follow-up visits will be done every 3 months for the first year, every 6 months for 2 years, then annually until death.

Included within this protocol are translational research, proteomics, FDG-PET and quality of life studies. Blood and tissue samples will be submitted from biopsy and resection specimens. Copies of pre- and post-induction scans will be submitted. Some of these studies are optional, and are specifically addressed in the consent form. ERCC1, XRCC1, TUBB-III and MAP4 are all genetic markers that have been associated with susceptibility or resistance to various chemotherapy agents. Levels of these markers will be correlated with patient outcomes. Shed Tumor DNA can be detected in patient plasma, and will be examined for a response to presence or lack of tumor.

Proteomic analysis by MALDI-TOF will be done to attempt to correlate several known proteomic patterns with patient outcome. FDG-PET data will be examined to define its usefulness in imaging the status of nodal disease in these patients.

**Progress:** This protocol remains open to enrollment with no patients enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205113	<b>Status:</b> Completed
<b>Title:</b> SWOG 9430, A Phase II Trial of Complete Surgical Resection for Stage IV Melanoma - Surgical Resection With Biological Evaluation And Clinical Follow-Up		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC		
<b>Start - Completion:</b> 11/30/2005 - Aug 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To assess the overall survival and progression-free survival of patients with metastatic melanoma (beyond the draining lymph nodes) following complete surgical resection of all known disease. (2) To determine the ability of the Southwest Oncology Group Melanoma Committee to enroll patients with metastatic melanoma who can be resected to a 'disease-free' state. This will assess the feasibility of future trials of specific interventions in this patient population.

**Technical Approach:** This study will enroll patients who have completely respectable metastatic melanoma who are appropriate for surgery alone. Clinical data will be collected to determine what clinical factors are associated with improved survival. Biologic samples for correlative studies on melanoma will be collected in the companion protocol SWOG 9431. A total of 100 eligible patients will enrolled on this study with up to two patients a year enrolled at MAMC. Patients will be consented and registered prior to surgery. Baseline evaluations include history and physical, laboratory tests, and disease assessment by CT, MRI or X-ray as appropriate. Follow-up after surgery will include physical exam, laboratory tests and disease assessment every 3 months for 1 year. The primary endpoint is survival. With 100 eligible patients, the one year survival rate can be estimated to within +/- 10%.

**Progress:** SWOG reported permanent closure of this protocol in December 2005, due to limited accrual over the past year. No subjects enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205114	<b>Status:</b> Completed
<b>Title:</b> SWOG 9431, Cytogenetic Molecular and Cellular Biology Studies in Metastatic Melanoma Patients, Ancillary		
<b>Principal Investigator:</b> LTC Tommy A. Brown, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC		
<b>Start - Completion:</b> 11/8/2005 - Aug 2010	<b>Funding:</b> SWOG via Henry M. Jackson Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To characterize the frequency of non-random cytogenetic abnormalities in regional and distant melanoma metastases and explore their association with clinical outcome of melanoma patients enrolled onto SWOG trials. (2) To characterize the frequency of specific genetic alterations at the DNA, mRNA, or protein level and explore the association of these abnormalities with clinical outcome in patients with regional and distant metastases who are enrolled on SWOG melanoma trials. The specific genes to be studied in this protocol include p16 and nm23. (3) To characterize the host immunologic response to metastatic melanoma by determining the whether the in vivo pattern of cytokine expression is consistent with specific subsets of T helper cells within melanoma deposits. To explore whether host immunologic response varies based on the site of metastatic disease and/or correlates with clinical outcomes in patients enrolled on SWOG trials. (4) To obtain peripheral blood, sera and paraffin embedded tumor blocks from patients with metastatic melanoma to create a tissue, cell and sera bank for future studies. (5) To attempt to correlate the most prevalent gene copy alterations observed in metastatic disease with the risk of progression in paraffin-embedded tissue samples collected in SWOG-9035 in patients with primary melanoma.

**Technical Approach:** This study plans to collect samples from patients enrolled in SWOG melanoma trials. Blood, serum, paraffin-embedded tissue and flash frozen tissue will be collected and stored to support future studies on the relationship of cytogenetics, immunological response, and genetic alterations in melanoma to patient outcomes. Enrollment in this study is a requirement for enrollment in the SWOG 9430 study of complete surgical resection in metastatic melanoma.

**Progress:** SWOG reported permanent closure of this protocol in December 2005, due to the closure of associated treatment protocols. No subjects enrolled at MAMC.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202013	<b>Status:</b> Ongoing
<b>Title:</b> Bariatric Surgery Effects on the Comorbidities of Obesity		
<b>Principal Investigator:</b> COL (Ret) Preston L. Carter, MD		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Craig S. See, MC; MAJ James A. Sebesta, MC; COL David M. Watts, MC; LTC Robert M. Rush, MC; Margaret I. Voelker, RN, CRC; MAJ Philip S. Mullenix, MC; COL Kenneth S. Azarow, MC; COL (Ret) William E. Eggebrotten, MD; MAJ Alec C. Beekley, MC; CPT Zachary M. Arthurs, MC; CPT Daniel G. Cuadrado, MC; CPT Katharine E. Wolcott, MC		
<b>Start - Completion:</b> 10/24/2001 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/26/2006

**Study Objective:** To determine and compare the effectiveness of resectional and laparoscopic gastric bypass in regards to reducing the comorbidities and mortality associated with morbid obesity.

**Technical Approach:** This study is a prospective observational study to analyze the effects of resectional and laparoscopic bypass on the morbidity and mortality of morbid obesity. All patients undergoing bariatric surgery at MAMC will be included in the study. A history, examination, and labs will be done preop, 3-6-and 12 months post-op. The variables and outcomes measured will include: weight, insulin/oral hyperglycemic requirement, fasting glucose, Hba1c, anti-lipid requirement, total cholesterol, LDL, HDL, triglycerides, antihypertensive requirement, blood pressure, sleep apnea screening questions, joint pain, panniculitis, hemoglobin, hematocrit, MCV, FE+, Ca+, vitamin B12, folate, prealbumin, and complications. Analysis of these outcomes of surgery will add significantly to the rationale behind bariatric surgery.

**Progress:** This prospective observational protocol remains open to patient entry, with 339 bariatric surgery patients enrolled, 127 during FY06. Ten patients withdrew prior to screening or having their surgical procedure. Data collection on enrolled patients continued at MAMC during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204001	<b>Status:</b> Ongoing
<b>Title:</b> Does Intestinal Fatty Acid Binding Protein Predict Strangulation in Mechanical Small Bowel Obstruction?		
<b>Principal Investigator:</b> CPT Daniel R. Cronk, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; CPT Troy P. Houseworth, MC; CPT Patrick M. McNutt, MS; COL Kenneth S. Azarow, MC; CPT Randy J. Kjorstad, MC		
<b>Start - Completion:</b> 10/24/2003 - Dec 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/10/2006

**Study Objective:** To determine if intestinal fatty acid binding protein (I-FABP) levels are elevated in patients with strangulated mechanical small bowel obstruction.

**Technical Approach:** This is a prospective, observational, pilot study investigating the utility of intestinal fatty acid binding protein (I-FABP) for detecting strangulated mechanical small bowel obstruction. Thirty consecutive patients presenting to the general surgery service with mechanical bowel obstructions will be enrolled and have plasma and urine I-FABP levels analyzed at the time of admission, time of operation, and 24 hours after operation (should they require operative intervention). Using multivariate analysis, levels of plasma and urine I-FABP will be compared between those patients without ischemia and those with ischemia upon operative exploration to determine if I-FABP is a potentially useful marker for the prospective identification of strangulated small bowel obstruction.

**Progress:** This protocol is open to patient entry, with no additional patients enrolled during FY06. Investigators plan to re-initiate enrollment within the next several weeks as more research personnel become available. To date, 45 subjects have been enrolled; 30 hospital patients with bowel obstructions (among these 3 "positives" that had ischemic bowel), ten normal controls and five dialysis patients.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206040	<b>Status:</b> Ongoing
<b>Title:</b> Does SDF-1 Production by Atherosclerotic Plaques Correlate with Severity of Carotid Artery Stenosis?		
<b>Principal Investigator:</b> CPT Daniel R. Cronk, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Garth S. Herbert, MC; COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC; MAJ Kelly S. Blair, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 1/5/2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/8/2006

**Study Objective:** To determine whether levels of SDF-1 as measured in atherosclerotic plaques correlates with the severity of disease.

**Technical Approach:** Blood will be drawn from patients scheduled to undergo carotid endarterectomy at the time of surgery or pre-operative evaluation to determine serum SDF-1 levels. In addition, a small section of plaque will be removed from the atherosclerotic plaque excised from twenty patients undergoing carotid endarterectomy at MAMC. The remainder of the plaque will be sent for routine pathological analysis (as is the standard at MAMC). The portion of the specimen used for study purposes will be brought to the Department of Clinical Investigation, where the presence of SDF-1 and possibly other inflammatory mediators will be established using immunohistochemical methods. Segments of radial artery harvested at the time of coronary artery bypass graft will be used as negative controls for immunohistochemical staining. Blood from healthy volunteers will be drawn for control values of serum SDF-1 levels. Regression analysis will be performed to attempt to determine a relationship between the level of SDF-1 in serum/plaques to the degree of carotid artery stenosis.

**Progress:** No patients have been enrolled to date. Responsibility for the bench portion of the study (immunohistochemistry and performance of ELISA) will likely be passed to a new research resident after submission of appropriate amendments. Clinical responsibilities have prevented the current investigators from initiating this study.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206041	<b>Status:</b> Ongoing
<b>Title:</b> Breast Abscesses Following Nipple Piercing: A Case Series and Review of the Literature		
<b>Principal Investigator:</b> CPT Daniel G. Cuadrado, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Alec C. Beekley, MC; COL (Ret) Preston L. Carter, MD		
<b>Start - Completion:</b> 1/5/2006 - Feb 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/8/2006

**Study Objective:** To review out institutional experience with the treatment of breast abscesses following nipple piercing.

**Technical Approach:** A chart review will be performed and patients separated into 2 groups based upon whether or not they have a pierced nipple on the infected side. Demographic data will be collected and analyzed between the two groups such as age, sex, date of piercing, date of surgery, number of surgical procedures and organism found in the abscess cavity. Data will be analyzed using a t-test for continuous and Chi square for categorical data.

**Progress:** Eight patients over the five year time period were identified who had abscesses due to nipple piercing. When compared to all breast abscesses treated operatively over that time, these patients had a significantly higher rate of requiring a second operation. An abstract was submitted to the Southwest Surgical Society for possible presentation and the work will be submitted for publication to the American Journal of Surgery during FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203114	<b>Status:</b> Completed
<b>Title:</b> Chewing Gum for the Reduction of Postoperative Ileus After Elective Open Colectomy		
<b>Principal Investigator:</b> CPT Daniel G. Cuadrado, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Daniel R. Cronk, MC; LTC Gregory P. Fitzharris, MC		
<b>Start - Completion:</b> 9/29/2003 - Nov 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/23/2005

**Study Objective:** To determine the efficacy of chewing gum at hastening the return of bowel function after major open abdominal surgery.

**Technical Approach:** This is a prospective, randomized, open-label trial evaluating chewing gum versus standard early resumption of oral intake for the reduction of postoperative ileus after open colon resection. A total of 36 consecutive patients ages 18-85 will be preoperatively randomized to receive either chewing gum or early oral intake starting on postoperative day number one.

Patients will record precisely the time of their first postoperative flatus and tolerance of solid food. Time to hospital discharge will also be evaluated. Time to first flatus, time to tolerance of solid food, and length of hospital stay will be compared between the two groups using student's t-test.

**Progress:** This protocol was reported completed with 29 of 38 subjects enrolled. Accrual was halted early because the Department of Surgery has made a move to primarily laparoscopic colon surgery and further enrollment would likely be limited at best. Data so far goes along with several recently published studies on the effects of gum; this small experience should add to the literature.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206016	<b>Status:</b> Terminated
<b>Title:</b> Determining the Incidence of Sonographically Detectable Wound Seromas in the Morbidly Obese: A Pilot Study		
<b>Principal Investigator:</b> CPT Daniel G. Cuadrado, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Katharine E. Wolcott, MC; CPT Matthew J. Eckert, MC; MAJ Joseph A. Ronsivalle, MC; MAJ James A. Sebesta, MC; COL (Ret) Preston L. Carter, MD		
<b>Start - Completion:</b> 10/28/2005 - May 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the rate of clinically significant and sub-clinically detectable wound seromas following open surgery in the morbidly obese.

**Technical Approach:** This descriptive study will examine the morbidly and super obese population (BMI 40-60) to determine the sonographic incidence of wound seromas following open bariatric surgery. Thirty consecutive obese patients undergoing bariatric surgery will be enrolled and undergo a pre-operative ultrasound of the planned surgical site by General Surgery Residents, in the pre-operative holding area, with the Sonosite® portable ultrasound to ensure that no pre-operative fluid collections are present. At the two week and one month post-operative visits, they will undergo repeat sonographic evaluation by a member of the research team. During the two and four week evaluation, the patients will have the length of their incision measured. At 2 cm intervals along the length of the incision (starting 4cm above and 4cm below the incision), consecutive measurements will be made to determine the width and depth of the fluid collection. The dimensions of the fluid collection will be tabulated and used to determine the area and volume of the seroma (Vellipse = length x width x depth x 0.5233). The presence or absence of wound infection or drainage from the wound will likewise be recorded. Any fluid collections identified will be brought to the attention of the attending surgeon. Standard treatment for symptomatic or infected seromas is drainage. Asymptomatic and subclinical seromas are normally followed, but this decision will be left to the attending surgeon.

All General Surgery residents obtain annual ultrasound training as part of the core curriculum. The sonographic examinations for this study will be performed only by the PI and AIs who will receive additional training from the Department of Radiology for the purposes of this study. Likewise, the images will be stored (labeled only with the code list identifier) so that the recorded measurements can be independently verified. The ultrasound device to be used will be the Sonosite from the General Surgery Clinic that residents are trained on.

**Progress:** The ultrasound device used could not get accurate reproducible pictures and more laparoscopic gastric bypass procedures are being performed compared to RGBs. This protocol was terminated during FY06, due to low accrual and it was no longer feasible to continue the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203034	<b>Status:</b> Ongoing
<b>Title:</b> Impact of Gastric Bypass with Subtotal Gastrectomy on Plasma Ghrelin Profile		
<b>Principal Investigator:</b> CPT Daniel G. Cuadrado, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Philip S. Mullenix, MC; COL Kenneth S. Azarow, MC; CPT Daniel R. Cronk, MC; CPT Craig S. See, MC; CPT Patrick M. McNutt, MS; COL (Ret) Preston L. Carter, MD; MAJ Alec C. Beekley, MC; CPT Zachary M. Arthurs, MC; CPT Garth S. Herbert, MC; CPT Katharine E. Wolcott, MC; LTC Matthew J. Martin, MC		
<b>Start - Completion:</b> 5/8/2003 - Dec 2003	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3/22/2005

**Study Objective:** To compare the preoperative, immediate postoperative, and 3 month postoperative plasma ghrelin profiles among a cohort of patients undergoing resectional gastric bypass (subtotal gastrectomy combined with roux-en-y bypass). To compare the pre and postoperative plasma leptin and insulin profiles among this patient cohort. To document the change in gross weight, body mass index, and blood pressure among this cohort.

**Technical Approach:** This study will prospectively compare the preoperative and postoperative levels of ghrelin, leptin and insulin in a cohort of patients undergoing resectional gastric bypass. Hormone levels will be obtained one day prior to surgery, two days after surgery, and at three to four months after surgery. Eighteen-hour profiles for each hormone will be generated and area under the curve calculated for comparison. Postoperative complications, amount of weight change, change in body mass index, and change in blood pressure will be recorded and analyzed. Statistical analysis will be done using two-tailed paired Student's t-test where appropriate.

**Progress:** This protocol remains ongoing, with 2 subjects enrolled. Based on recent published data with Ghrelin, investigators plan to revise the original protocol and change the total number of blood draws to four. This would be a major reduction in the amount of blood draws and reduction in the risk of the procedure.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206047	<b>Status:</b> Completed
<b>Title:</b> Bronchoscopy in the Blast Injury Patient		
<b>Principal Investigator:</b> CPT Matthew J. Eckert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 1/24/2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The purpose of this study is to evaluate respiratory symptom development and fiberoptic bronchoscopy findings in a series of blast injured patients in Operation Iraqi Freedom (OIF).

**Technical Approach:** This study is a retrospective review of tourniquet use among all patients with major extremity injuries who presented to the 31st Combat Support Hospital in Iraq, in support of Operation Iraqi Freedom. An existing database of approximately 30 subjects will be reviewed. Collected data includes mechanism of injury, type of blast, associated burns, and requirement for endotracheal intubation, vital signs, time sequence between point of injury and presentation of pulmonary injury symptoms, therapeutic interventions performed, and bronchoscopic findings. Statistical analysis will be performed to examine whether therapeutic intervention prevented the need for endotracheal intubation and to identify variables associated with requirement for intubation. Conclusions will help to better inform medical personnel treating blast injury patients of the incidence and associated injury pattern in those patients with delayed airway injury manifestation, and the time interval between injury and delayed symptom development.

**Progress:** This review of 23 blast injured Soldiers demonstrated that delayed manifestation of secondary airway injury may require up to 18 hours of observation in an acute care setting due to the significant incidence of delayed airway edema symptoms in this population. The results of this study were presented at the annual meeting of the Pacific Coast Surgical Association, 19 Feb 2006, and were awarded "Best Resident Paper Competition" winner. The manuscript was published in Aug 2006 Archives of Surgery.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206115	<b>Status:</b> Ongoing
<b>Title:</b> Hypoxemic Reperfusion Following Lower Torso Ischemia in sp. <i>Sus scrofa</i>		
<b>Principal Investigator:</b> CPT Matthew J. Eckert, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; CPT Vance Y. Sohn, MC; CPT Jason T. Perry, MC		
<b>Start - Completion:</b> 8/9/2006 - Aug 2009	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Hypothesis is that hypoxemic reperfusion (PaO<sub>2</sub> 30-35mmHg) compared with normoxemic reperfusion (PaO<sub>2</sub> 100mmHg) following lower torso ischemia induced by supra-celiac aortic cross-clamping results in improved hemodynamic stability and pulmonary gas-exchange, decreased vasoactive medication requirements, decreased reperfusion injury induced histopathologic changes in multiple organ systems, and less evidence of reactive oxygen species activity. Additionally, hypothesize that the hypoxemic reperfusion strategy will limit the hind-leg compartment pressure compared to normoxemic reperfusion.

**Technical Approach:** V.1. Experimental Design and General Procedures: This experiment will be conducted in a multi-phase format, beginning with a pilot study to determine the feasibility of our model. This general protocol will cover the basics of the overall experimental goal, but subsequent amendments will detail successive phases as dictated by success of the pilot study and refinement of various techniques.

**Phase I (Pilot Study):** The pilot study will utilize a total of four pigs. After establishment of general anesthesia, arterial vascular access will be obtained for continuous pressure monitoring at the common carotid or femoral artery using a cut-down approach and Seldinger cannulation technique. Hind leg compartment pressure will be monitored continuously using an arterial catheter placed percutaneously into a hind-leg musculo-fascial compartment. Venous access via the jugular vein will be obtained for intra-venous fluid and medication administration. An additional lower extremity vein (likely femoral vein) will be accessed for sampling of the ischemic region of the body. Ventilatory parameters will be adjusted to maintain baseline blood gas parameters during the access and ischemia portions of the experiment (PaO<sub>2</sub> 70-90mmHg, PCO<sub>2</sub> 40-50, pH 7.4-7.55 and saturations of 92-98%) After baseline stabilization and laboratory analysis (blood gas, lactate, chem.-7 panel), a midline laparotomy will be performed with cross-clamping of the supra-celiac aorta for 60 minutes. A supra-pubic bladder catheter will be placed to allow for measurement of urine production during the ischemic and reperfusion phases. Prior to the end of 60 minutes of ischemia repeat lab samples will be performed. During the last 10 minutes of ischemia ventilatory management will alter the PaO<sub>2</sub> to a goal of 30-35mmHg by decreasing the fraction of inspired O<sub>2</sub> (FiO<sub>2</sub>), for the hypoxemic reperfusion group (HR). The normoxemic reperfusion group (NR) will enter the reperfusion phase with a goal PaO<sub>2</sub> of 95-105mmHg. Once these ventilatory parameters are met, the cross-clamp will be released, with serial hemodynamic measurements every 15 minutes during the 120 minute reperfusion phase with repeat lab sampling every 30 minutes and continuous compartment pressure monitoring. During the ischemic and reperfusion phase lactated ringer's fluids and epinephrine will be used as needed to maintain the baseline MAP (Douzinias et al. Crit Care Med 2003;31:2183 found that 50ug/min i.v. epinephrine just prior to cross-clamp release and as need thereafter prevented immediate cardiac arrest). The total intra-venous fluid and pressor medication requirements will be recorded for comparison. The protocol of ventilatory management for the HR group during the reperfusion phase is as follows: 10 minutes of a goal PaO<sub>2</sub> of 30-35mmHg, followed by gradual increase of the FiO<sub>2</sub> to achieve a goal PaO<sub>2</sub> of 50mmHg at 60 minutes reperfusion and finally 100mmHg at 120

minutes of reperfusion. Following reperfusion completion and final lab/hemodynamic value recording, the animals will be euthanized.

V.1.2. Phase II: Following confirmation of our experimental model from Phase I, we plan to conduct a full trial of hypoxemic vs. normoxemic reperfusion with additional biochemical and pathologic analysis evaluating the activity and effects of reactive oxygen species. The ischemia-reperfusion model will be identical unless found to require modification during the pilot and appropriately addressed in an addendum. Phase II will include post-mortem tissue sampling of lung, liver, kidney and brain for histopathologic evidence of ischemia/inflammatory changes. This will be conducted by two pathologists unaware of the animal's reperfusion strategy, with organ injury graded by a predetermined scale. Inter-observer variability will be calculated. Additional biochemical analysis during Phase II will include measurement of free radical activity and effects. This will be conducted using venous whole blood samples with commercially available kits for oxygen free radical activity and superoxide dismutase (Trevigen, Gaithersburg, MD) assays, along with determination of xanthine oxidase activity (Invitrogen, USA). The detrimental effects of lipid peroxidation by free radicals will be determined with malonaldehyde (MDA) and hydroxyalkenal assays of whole blood samples (Calbiochem, San Diego, CA). We tentatively plan to use a total of 20 pigs during Phase II, ten in each group. We reserve the right to change the commercial assay kits if a cheaper, equivalent product is found in order to reduce the cost of this experiment. Such changes would be detailed in subsequent amendments as needed.

V.1.3. Phase III: Phase III is a potential further experimental trial evaluating the beneficial effects of known free radical scavengers (mannitol, allopurinol, superoxide dismutase) in concert with a hypoxemic reperfusion strategy for improved control/modulation of the reactive oxygen species contribution to reperfusion injury. This Phase will be addressed in a future amendment pending successful completion of Phase I/II and statistical analysis to determine the number of animals required to show a significant difference between treatment groups.

**Progress:** Protocol was recently approved, will begin in FY 2007.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205080	<b>Status:</b> Ongoing
<b>Title:</b> Stem cell engraftment in the lipopolysaccharide mouse (Mus musculus) model of acute inflammatory injury		
<b>Principal Investigator:</b> CPT Matthew J. Eckert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Daniel R. Cronk, MC; CPT Daniel G. Cuadrado, MC; CPT Kerry L. O'Brien, MC; COL Kenneth S. Azarow, MC; CPT Garth S. Herbert, MC		
<b>Start - Completion:</b> 5/11/2005 - May 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/10/2006

**Study Objective:** To investigate the most efficient conditions under which to administer stem cells to mice following experimentally induced inflammatory injuries.

**Technical Approach:** This study will be carried out in four phases. The first phase will be a pilot study to develop the LPS injury model in this laboratory, to further characterize a number of molecules that play a role in stem cell movement but have not been studied in LPS injury, and to accurately define the optimal timing for administration of cellular therapies to enhance their eventual engraftment in the target tissue. LPS injuries in the lung and skeletal muscle will be utilized. The first phase will also involve in vitro studies of the cultured bone marrow from mice euthanized during this first phase. The in vitro studies will allow us to evaluate cell culture treatments that may enhance the administered stem cells. To date, the pulmonary LPS injury has been demonstrated reproducibly in our lab from our previous studies. To complete phase 1 similar LPS challenges in skeletal muscle will be performed. This will be accomplished by intramuscular injection of LPS with animal sacrifice at 0, 6, 12, 24, 48 and 72 hours. The muscle samples will be analyzed by histology, immunohistochemistry and ELISA. The second phase of this study will involve using various pro and anti-inflammatory cytokines to modulate the local immune response following LPS induced injury. To date in our lab we have demonstrated that stromal derived growth factor 1 (SDF-1) is modulated following LPS induced lung injury. This cytokine has been previously demonstrated to be essential for stem cell engraftment following bone marrow transplant. In order to further characterize the role of SDF-1 in inflammatory injury, we will measure tissue levels following LPS challenge. Furthermore, through the use of cytokine delivery systems we will characterize the effect of dyschronic administration of SDF-1 on the inflammatory cascade. Using 100 micron heparin sulfate bonded acrylic beads injected into the subcutaneous tissue (along with bupivacaine to reduce pain) we will examine the cellular response both in the presence as well as in the absence of LPS. The third phase of this study will involve transplantation of bone marrow into LPS injured mice and evaluation of engraftment into target tissues at various time points. For this phase of the protocol, LPS will be administered through either direct injection (i.e. intratracheally, intraperitoneally) or through a subcutaneous delivery system in the thigh (heparin sulfate impregnated beads). The fourth phase of this study will combine information from the first three phases and determine if the putatively successful maneuvers evaluated in phase one actually enhance engraftment of transplanted bone marrow cells.

**Progress:** This multi-phase project evaluating the effects of intra-peritoneal and intra-tracheal LPS inoculation with regard to SDF-1 modulation continues, with good confirmatory results from a second trial of IP inoculation. The results of the IT-LPS study were submitted to a major journal for publication and we are currently preparing the IP-LPS results for submission as well. The next phase of the project will utilize proteomic micro-array techniques to identify any associated molecules related to SDF modulation. A separate amendment will be submitted next with details of the upcoming steps in this project.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204101	<b>Status:</b> Terminated
<b>Title:</b> Advanced Trauma Life Support (ATLS) Training Utilizing the Goat (Capra hircus)		
<b>Principal Investigator:</b> COL (Ret) William E. Eggebroten, MD		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 7/14/2004 - Jul 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/12/2005

**Study Objective:** To administer life saving care to trauma patients e.g. insertion of chest tube, cricothyroidotomy, pericardiocentesis or diagnostic peritoneal lavage. This training will teach physicians one safe method of performing these life saving procedures for trauma patients, as well as optional venous cut-down. The use of animals will enhance the clinical skills and confidence of the trainees during the training session. This will result in improved patient care during a critical, emergency situation. Live animals are preferred in order to provide the closest simulation to the real life-saving situation possible. Human cadavers and simulators have been used in the past and have been judged to be less realistic. The new Sim-Man (registered trademark) simulator promises to more closely resemble simulation of the life-saving procedures and the ACS is transitioning to this simulated model for its ATLS student courses. Cost considerations of approximately an additional \$2500 per course for use of this product must be recognized and for this reason the faculty judge the Sim-Man an acceptable alternative to the live animal model when additional funding has been secured in the future.

**Technical Approach:** The ACS has developed a copyrighted course designed to educate physicians in the basics of trauma care. As part of a 2-day course, an animal training module will be incorporated. After the animals are adequately anesthetized, each procedure will be performed as described below. A suitable vein is selected on the leg and an incision is made over it. The vessel is isolated and a plastic catheter is placed inside of it. This allows fluid to be given rapidly. Next, a diagnostic peritoneal lavage is performed. A small incision is made on the lower abdomen and a long catheter is inserted into the abdominal cavity. Fluid is infused into the abdomen and then removed for laboratory analysis. This allows the identification of intra-abdomen injury. Following this, chest tube insertion is performed. This is accomplished by making a 1-2 inch incision on the lower chest. A clamp is then bluntly placed through the space between the ribs into the chest cavity. A large tube is placed through this hole, allowing drainage of fluid/blood and re-expansion of a collapsed lung. Pericardiocentesis is performed by placing a long needle through the chest wall into the sac surrounding the heart. This allows removal of any blood that may be compressing the heart. Prior to pericardiocentesis, the pericardium is filled with fluid by placing a catheter within the pericardium. An anterolateral, left sided thoracotomy is performed by making an incision in the left, fifth intercostal space extending from the sternum to the posterior axillary line. All subcutaneous tissue, muscles and pleura are dissected with scissors or a scalpel. Rib retractors are placed to gain exposure. The pericardium is identified and incised. The catheter is sutured into place and the pericardium is filled with fluid. Next a cricothyroidotomy is performed by making an incision over the windpipe into the neck. Next, a cricothyroidotomy is performed by making an incision over the windpipe into the neck. An incision is then made into the windpipe. A tube is placed through the incision into the wind pipe in order to breathe for the patient. The animal is euthanized prior to performing the cricothyroidotomy.

**Progress:** No labs run in FY 2005 or FY 2006, ATLS is using TraumaMan (non-animal alternate) instead of live animal models. Protocol is terminated.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204100	<b>Status:</b> Ongoing
<b>Title:</b> Human Blood Collection for Bench Research Initiatives		
<b>Principal Investigator:</b> CPT Michael J. Hartenstine, MS		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Daniel G. Cuadrado, MC; CPT Daniel R. Cronk, MC; CPT Patrick M. McNutt, MS; CPT Garth S. Herbert, MC		
<b>Start - Completion:</b> 7/16/2004 - Jul 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** To obtain blood samples from normal, healthy subjects for use in bench experiments involving the behavior of blood cells in culture. To obtain blood samples from normal, healthy subjects for use as controls in bench experiments (e.g., ELISA analyses).

**Technical Approach:** Prospective collection of tissue samples with subjects selected by announcements asking for volunteers at meetings within DCI and DOS. Blood will be aseptically obtained in an amount not to exceed 550ml from any one subject in any 8-week period. Not more than two blood draws will be performed on any one subject in any one week period. Blood will either be used immediately for bench experiments, or frozen and stored for use at a later date. Samples will be de-linked from subjects at the time of blood draw. No additional information will be obtained from subjects. Samples will not be transported out of the DCI. Samples will be destroyed within one year of collection.

**Progress:** This protocol remains available to collect blood samples to be used as a source of cells and other substances e.g. proteins from healthy subjects. One subject has enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206026	<b>Status:</b> Ongoing
<b>Title:</b> Determination of Telomerase Activity in Atypical Ductal Hyperplasia of the Breast		
<b>Principal Investigator:</b> CPT Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC; MAJ Anne L. Champeaux, MC; CPT Matthew J. Eckert, MC; CPT Michael J. Mulcahy, MC		
<b>Start - Completion:</b> 12/14/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objective is to determine the presence and prognostic significance of telomerase activity in breast atypical ductal hyperplasia.

**Technical Approach:** A review of Breast pathway charts will be completed to identify 20 patients with a diagnosis of atypical ductal hyperplasia on core biopsy who went on to open surgical biopsy. Ten of these patients will have ductal carcinoma in situ (DCIS) identified at open surgical biopsy and ten will have benign pathology. Data will be coded and immunohistochemistry performed on the paraffin slides of these tissues. The pathologic diagnosis on open surgical biopsy will be compared and correlations made (if any) between intensity of staining and the presence/absence of cancer on open surgical biopsy.

**Progress:** This bench protocol identified seventeen patients who underwent open surgical biopsy following core biopsy that showed ADH. Testing was performed on old surgical specimens. Telomerase staining was not predictive of which patients with ADH on core biopsy would go on to have cancer on open surgical biopsy. A manuscript has been prepared for presentation at the North Pacific Surgical Association meeting, and is being forwarded to DCI for review.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206010	<b>Status:</b> Ongoing
<b>Title:</b> Does Control of Inflammation Prior to Intervention for Carotid Artery Disease or Lower Extremity Peripheral Arterial Disease Affect Outcome?		
<b>Principal Investigator:</b> CPT Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 2/6/2006 - Jul 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/19/2006

**Study Objective:** This study will determine the effect that a 30-day course of aspirin and statins have on inflammation, as measured by CRP levels and determine whether peri-operative management of inflammation affects outcome (specifically re-stenosis / myointimal hyperplasia) following intervention for Carotid Artery Stenosis or Peripheral Arterial Disease.

**Technical Approach:** Participants in this study will include up to 200 volunteers who require intervention for CAS, in addition to 120 who require intervention for lower extremity PAD. Patients will be randomized to either intervention alone (surgery or angioplasty/stenting) accompanied by moderate statin therapy (standard of care for patients with atherosclerotic disease), or a 90-day peri-operative course of atorvastatin and aspirin directed at reducing the degree of systemic inflammation (to include 30 days pre-operatively and 60 days post-operatively). CRP levels will be measured in each group at baseline, pre-operatively, and during follow up visits. Subjects will undergo surgery for carotid artery stenosis, or intervention for lower extremity PAD. Complications, to include myocardial infarction, stroke, death, and in particular, re-stenosis will be measured in each group. The number of complications in each group (those simply undergoing surgery, and those who have surgery accompanied by a 90-day regimen of anti-inflammatory medications) will be compared to determine whether control of inflammation has an impact on outcome of intervention for carotid artery stenosis or peripheral arterial disease.

**Progress:** This protocol remains open to patient entry; however, many of the patients who were undergoing intervention for carotid artery stenosis or infrainguinal peripheral vascular disease were already taking high doses of statins (exclusion criteria). Other patients could not wait 30 days prior to the required intervention, which is necessary time for the anti-inflammatory therapy of statin / ASA to show an effect. Investigators plan to revisit the inclusion criteria and possibly amend the protocol as necessary to facilitate enrollment.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201020	<b>Status:</b> Ongoing
<b>Title:</b> Learning Curves for Airway Assessment and Endotracheal Intubation - Cumulative Sum Analysis		
<b>Principal Investigator:</b> CPT Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC; LTC Joseph P. Miller, MC; MAJ James A. Sebesta, MC; CPT James C. Nunley, MC; LTC Gregory P. Fitzharris, MC; CPT Craig S. See, MC; MAJ Jennifer E. Jorgensen, MC; LTC Ronald J. Place, MC; CPT Jeffrey S Kunz, MC; LTC Alan L. Beitler, MC; CPT Amy L. Young, DO		
<b>Start - Completion:</b> 11/28/2000 - Jul 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/26/2006

**Study Objective:** (1) To evaluate individual and institutional learning curves for airway assessment by analyzing diagnostic accuracy as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, (2) To develop individual and institutional learning curves for the skill of endotracheal intubation as a function of experience for a group of surgical interns performing a 4-week rotation on the anesthesia service, and (3) To evaluate a model (Cumulative sum analysis) for assessing the technical proficiency of surgical interns in the skills of airway assessment and endotracheal intubation.

**Technical Approach:** Surgical interns will receive standardized training on airway anatomy and assessment coupled with a practical session on intubation in ATLS models. These house officers will then perform airway assessments and endotracheal intubations on surgical patients who are 18 years or older, ASA class I or II, and who do not require rapid sequence intubation. Each attempt will be supervised and scored by a staff anesthesiologist or CRNA using a standardized data sheet. A successful assessment will be one where the airway classification matches the supervising staff's determination. A successful intubation will be insertion of an endotracheal tube within 30 seconds of laryngoscopy initiation, documented by end tidal CO<sub>2</sub>. If an attempt is unsuccessful, the process may be repeated. Each consecutive attempt will be recorded separately. A data sheet will be filled out and a new score assigned for each attempt, even when there are multiple attempts on a single patient. Supervising staff will determine if and when they need to step in and intubate the patients themselves.

Data sheets will be turned in to the principal investigator, who will calculate CUSUM values and plot learning curves. Data will be monitored during the rotation. At the completion of the 4-week experience, these results will be shared with the interns and staff. After an entire class of interns has completed the rotation, the results will be submitted for publication and presentation.

**Progress:** This protocol remains ongoing with five additional subjects enrolled during this fiscal year. Additional efforts were taken to ensure data was retrieved on all surgical interns rotating through anesthesia, but investigators were not successful in capturing data from all potential subjects. Data has already been published on the endotracheal intubation portion of the learning curve assessment. There are no plans to accrue a significant number of subjects to further enhance the results in this portion of the protocol. Efforts will be focused in the next year towards assessing the benefit of colonoscopy simulators in preparing interns for real colonoscopies (prepared as an amendment to this protocol). An associate investigator will be added to assist with data collection as he is currently working with surgical residents at the Andersen Simulation Center.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206027	<b>Status:</b> Ongoing
<b>Title:</b> Prognostic Significance of Telomerase Activity in T1 and T2 Rectal Adenocarcinoma for Patients Undergoing Transanal Excision		
<b>Principal Investigator:</b> CPT Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 12/14/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/8/2006

**Study Objective:** To determine the presence and prognostic significance of telomerase activity in rectal adenocarcinoma for patients who undergo trans-anal excision of these lesions.

**Technical Approach:** Madigan Army Medical Center operative charts will be reviewed to identify 20 patients with a diagnosis of rectal adenocarcinoma who have undergone transanal excision. This data will be coded and immunohistochemistry performed on the paraffin slides of these tissues. Clinical outcome data will be compared in an attempt to make correlations between the degree of telomerase activity and pathologic stage, as well as with the incidence of recurrence. Telomerase activity may prove to be prognostic indicator of which patients should undergo more aggressive surgery in the management of rectal adenocarcinoma.

**Progress:** This bench protocol identified fourteen patients who previously underwent trans-anal excision of rectal cancer. Testing was performed on old surgical specimens. Currently there are insufficient numbers to determine whether positive staining for telomerase is predictive of whether tumors will recur. Investigators will attempt to identify other patients who have undergone transanal excision in order to have sufficient power to determine whether telomerase staining is a worthwhile procedure in evaluating rectal cancer.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205125	<b>Status:</b> Ongoing
<b>Title:</b> Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Delayed Gastric Emptying after Pancreaticoduodenectomy		
<b>Principal Investigator:</b> CPT Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 1/9/2006 - Sep 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/28/2006

**Study Objective:** To determine the efficacy of Tegaserod for relief of delayed gastric emptying after pancreaticoduodenectomy.

**Technical Approach:** 70 TRICARE beneficiaries scheduled to undergo pancreaticoduodenectomy will be asked to enroll. Subjects will be randomized to receive either placebo or Tegaserod 6 mg, orally, twice a day once oral intake is allowed following pancreaticoduodenectomy. Subjects will be monitored for evidence of delayed gastric emptying and return of bowel function (flatus, bowel movements). The time between surgery and discharge will also be recorded. The percentage of patients in each group with delayed gastric emptying will be compared using the Mann-Whitney test to determine whether Tegaserod provided any benefit in reducing the incidence of DGE.

**Progress:** This protocol is open to enrollment, no patients enrolled to date.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205126	<b>Status:</b> Ongoing
<b>Title:</b> Prospective, Randomized, Placebo-Controlled Trial of Tegaserod for Treatment of Post-Operative Ileus Following Partial Colectomy		
<b>Principal Investigator:</b> CPT Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC		
<b>Start - Completion:</b> 1/9/2006 - Sep 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/26/2006

**Study Objective:** To determine the efficacy of Tegaserod for amelioration of post-operative ileus following partial colectomy

**Technical Approach:** 60 TRICARE beneficiaries scheduled to undergo partial colectomy will be asked to enroll. Subjects will be randomized to receive either placebo or Tegaserod 6 mg orally, twice a day beginning the day following surgery. Data will be collected on length of hospital stay, time between surgery and first flatus, first bowel movement, and the time until tolerating a regular diet. The average hospital stay will be compared between the control and study groups using the Student's t-test.

**Progress:** This protocol remains open to patient entry, with eight patients enrolled. One patient was unblinded due to a concern for anastomotic ischemia prior to being taken back to the operating room. The patient was found to be on placebo. No analysis will be attempted to date; 7/8 patients remain blinded.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205063	<b>Status:</b> Ongoing
<b>Title:</b> The Impact of Nodal Micrometastases on Survival of Women with Breast Cancer		
<b>Principal Investigator:</b> CPT Garth S. Herbert, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 4/6/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3/21/2006

**Study Objective:** To establish whether the presence of nodal micrometastases in breast cancer is predictive of a worse outcome.

**Technical Approach:** This study is a retrospective review of all women diagnosed with breast cancer at MAMC between 1996 and 2003. Survival and disease-free survival will be compared in patients with benign lymph nodes and those with microscopic evidence of metastasis (tumor foci < 2mm and diagnosed by hematoxylin and eosin stain or immunohistochemistry). Other potential investigations include (but are not limited to) analysis of the sensitivity of touch prep for analysis of sentinel lymph nodes at MAMC, and survival in patients with metastasis to the sentinel lymph node who do or do not have an axillary dissection.

**Progress:** This retrospective chart review protocol remains ongoing. Over 400 patient charts were reviewed, but only sixteen patients were identified with isolated tumor cells detected in lymph nodes. Patient and tumor characteristics, as well as recurrence and survival rates were compared to women with node negative disease. A difference was not detected in recurrence or survival rates in patients with isolated tumor cells. Results will be presented at the North Pacific Surgical Association, and a manuscript is being forwarded to DCI.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202073	<b>Status:</b> Terminated
<b>Title:</b> Ultrasound Imaging for Central Venous Catheter Placement in the Intensive Care Unit: Is Real-time Really Better? A Prospective Randomized Trial		
<b>Principal Investigator:</b> CPT Farah A. Husain, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Philip S. Mullenix, MC; CPT Michael Piesman, MC; MAJ Scott R. Steele, MC; LTC Matthew J. Martin, MC; LTC Leonard E. Deal, MC		
<b>Start - Completion:</b> 10/16/2002 - Dec 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/24/2005

**Study Objective:** (1) To compare three methods of internal jugular central venous catheter placement in a prospective randomized fashion: anatomic landmarks only, ultrasound to evaluate the anatomy and mark the site, real-time ultrasound guidance. (2) Determine if internal jugular vein diameter is predictive of successful line placement and/or complications. (3) Analyze cost-effectiveness of using ultrasound for central line placement. (4) Analyze effect of patient factors such as age, body mass index, and coagulopathy and prior same-site central lines on successful central venous catheter placement and complication rate. (5) Analyze effect of operator factors such as training level, department (medicine, surgery, emergency medicine, etc.) and prior experience on successful central venous catheter placement and complication rate.

**Technical Approach:** In this study we will prospectively compare 3 different methods of internal jugular central venous catheter placement in 100 consecutive patients by random assignment: anatomic landmarks only, ultrasound to evaluate the anatomy and mark the site, real-time ultrasound guidance. We will examine data relating to patient factors including age, body mass index, previous central lines, and coagulopathy. We will also examine procedural data for each method to include number of needle passes, complications, success or failure of line placement, time of procedure, and internal jugular vein diameter. There will be no long term or outcome data studied. The 3 methods will then be compared for any statistically significant difference in ease of line placement, incidence of complications, and success rates. Data will also be analyzed by resident year group, experience level, and department of origin. Statistical analysis will be done using Student's t-test, analysis of variance, and chi-square or Fisher's exact test where appropriate.

**Progress:** This study was terminated in September 2006, when the current PI left MAMC and the remaining study investigators felt continuation of the protocol would not be feasible. During the four years of active study enrollment only 40 of 108 subjects were enrolled. No data analysis was conducted.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206043	<b>Status:</b> Ongoing
<b>Title:</b> Colorectal Complications of External Beam Radiation vs. Brachytherapy for Prostate Cancer		
<b>Principal Investigator:</b> CPT Randy J. Kjorstad, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Matthew J. Martin, MC; MAJ Philip S. Mullenix, MC; LTC John B. Halligan, MC; MAJ Scott R. Steele, MC; 2LT Richard N. Lesperance, MC		
<b>Start - Completion:</b> 1/9/2006 - Feb 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** The objective is to determine the prevalence and significance of colorectal complications (i.e. bleeding, ulceration, proctitis, incontinence) following external beam radiation therapy versus brachytherapy for prostate cancer.

**Technical Approach:** A chart review of all cases of each modality will be performed and colon and rectal complications compared as well as functional outcome for each approach. Records in the radiation oncology clinic will be used to generate the patient names for each of the two methods. Data will be collected and organized on an excel spreadsheet for analysis.

**Progress:** Retrospective data on 288 MAMC patients who received external beam radiation therapy (EBRT) was collected during FY06. Data analysis is being conducted; although, no conclusions have been made thus far. Following completion of data analysis, investigators will decide if it is suitable to proceed with publication with the current number of patients or seek collaboration with other military treatment facilities, extending the protocol into a multisite study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205127	<b>Status:</b> Terminated
<b>Title:</b> Screening for Occult Vascular Injuries Utilizing a Portable Ultrasound Unit		
<b>Principal Investigator:</b> CPT Randy J. Kjorstad, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Zachary M. Arthurs, MC; CPT Garth S. Herbert, MC; COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 2/2/2006 - Jul 2007	<b>Funding:</b> TATRC via MIPR	<b>Periodic Review:</b> 8/23/2006

**Study Objective:** To determine whether a portable ultrasound can be used to identify occult vascular pathology and the feasibility of using it in a trauma evaluation.

**Technical Approach:** This will be a biphasic study to first validate a new ultrasound machine with resident operation on known pathology, then to translate this technology to the trauma setting. This data will then be compared to reported data on the sensitivity and specificity of color flow doppler for the diagnosis of vascular pathology. The portable ultrasound utilized in this study will be a noncommercial machine developed by the staff of Worcester Polytechnic Institute.

Phase I will consist of general surgery and emergency medicine residents utilizing the portable ultrasound to evaluate ankle-brachial indices and localize segments of vascular disease in patients with known vascular pathology. Volunteer patients with suspected vascular pathology scheduled to undergo arteriography will be used in this phase only to validate the portable ultrasound's accuracy and to develop the resident's skills in identifying pathology. The data gained will be compared with reported sensitivities and sensitivity of the standard commercially available color flow Doppler machines ran by trained vascular laboratory technicians.

Phase II will utilize all patients undergoing evaluation of blunt or penetrating extremity trauma at the emergency room at MAMC. This would consist of an ABI and further ultrasonic investigation if the ABI<.95. This will be a screening exam only. No clinical decisions will be made on the information gained from this exam. All findings will be correlated with formal ABI, duplex ultrasonography, and arteriography if required by current treatment algorithms. The study results will be compared the published current sensitivity and specificity of color flow doppler in the diagnosis of vascular injuries to confirm the hypothesis.

**Progress:** This protocol was terminated due to technical difficulties with the portable ultrasound. No patients were enrolled in the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206079	<b>Status:</b> Ongoing
<b>Title:</b> The Utility and Impact of Standard Trauma Triage Criteria in the Elderly		
<b>Principal Investigator:</b> LTC Matthew J. Martin, MC		
<b>Department:</b> Surgery/General Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Ryan K. Lehmann, MC; CPT Matthew J. Eckert, MC		
<b>Start - Completion:</b> 4/13/2006 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To analyze and compare the trauma triage criteria and implementation as well as outcomes among elderly (age>65) trauma victims in the State of Washington.

**Technical Approach:** This is a retrospective study utilizing pooled data collected from several different hospitals in the State of Washington over a four year period and placed on a database. Variables pertaining to patient age, length of stay, ICU admission, and trauma scores will be evaluated for possible trends/correlation between age and outcomes from trauma victims.

**Progress:** The full database from the Washington State Department of Health has been obtained; data analysis is planned to begin in December 2006. Preliminary results and an abstract are likely to be submitted to a national meeting by May 2007. The initial data analysis was delayed due to the deployment of the primary investigator, but should now proceed as planned.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203091	<b>Status:</b> Terminated
<b>Title:</b> Prospective Evaluation Of Intraoperative Duplex Ultrasound As An Adjunct To Technical Excellence During Carotid Endarterectomy		
<b>Principal Investigator:</b> MAJ Philip S. Mullenix, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; CPT Zachary M. Arthurs, MC; CPT Garth S. Herbert, MC; CPT Craig S. See, MC; LTC Benjamin W. Starnes, MC; CPT Katharine E. Wolcott, MC; CPT Daniel G. Cuadrado, MC; MAJ Scott R. Steele, MC; LTC Matthew J. Martin, MC; LTC Neal C. Hadro, MC		
<b>Start - Completion:</b> 7/1/2003 - Dec 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/14/2005

**Study Objective:** To prospectively evaluate in an observational fashion the relationship between intraoperative duplex ultrasound (duplex) findings and subsequent neurologic outcomes and re-stenosis rates among patients undergoing carotid endarterectomy (CEA). To prospectively evaluate in an observational fashion our duplex criteria for immediate revision of endarterectomy.

**Technical Approach:** This is an observational prospective cohort study designed to evaluate the relationship between intraoperative duplex ultrasound findings and subsequent neurologic outcomes and re-stenosis rates among 120 patients undergoing carotid endarterectomy, and to prospectively evaluate our duplex criteria for immediate revision of endarterectomy. The study represents no deviation from the current standard of care at this facility and involves no additional procedures, medications, or interventions above that already being provided as part of the treatment of the patient's disease process.

**Progress:** This protocol was terminated by the PI in June 2006, with no subjects enrolled. Initiation of the protocol was not possible due to time constraints.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206061	<b>Status:</b> Ongoing
<b>Title:</b> Utilization of Genetic Testing and Counseling Among Patients with Hereditary Non-Polyposis Colorectal Cancer		
<b>Principal Investigator:</b> CPT Jason T. Perry, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 2/7/2006 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To describe rates of utilization of genetic testing and counseling (GTC) among patients diagnosed with hereditary non-polyposis colorectal cancer (HNPCC) and further characterize use of recommended screening/surveillance studies after receiving GTC.

**Technical Approach:** Patients contained in the Madigan colorectal cancer database (from its inception in 1995 to present) and meeting the Amsterdam criteria II criteria will be extracted. The uptake of genetic testing and counseling will then be derived by reviewing patient medical records (including pathology results contained within the CHCS), and patient records from Medical Genetics. This study will further attempt to characterize patients' adherence to recommended screening guidelines and or surgical interventions follow testing and counseling in comparison to patients that did not accept testing or counseling.

**Progress:** This protocol is still in the data acquisition phase and no conclusions are available at this time.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206038	<b>Status:</b> Ongoing
<b>Title:</b> Venous Distensibility Index as a Predictor of Radiocephalic Arteriovenous Fistula Maturation		
<b>Principal Investigator:</b> CPT Jason T. Perry, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC; COL Howard M. Cushner, MC		
<b>Start - Completion:</b> 1/5/2006 - Jul 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objective is to determine whether venous compliance, as measured by a venous distensibility index (VDI), is associated with an increased rate of arteriovenous fistula (AVF) maturation.

**Technical Approach:** 50 patients with end-stage renal disease referred to Vascular Surgery for consideration of permanent hemodialysis vascular access will be offered enrollment in this study. Venous distensibility index will be determined by modifying the preoperative ultrasound protocol already utilized in every dialysis candidate in whom an arteriovenous fistula is considered. In addition to collecting historic (e.g. duration and etiology of end-stage renal disease), physiologic (creatinine clearance, HbA1c), morphologic data (vein calibers, venous distensibility index), patients will be followed to determine the rate of maturation at six weeks and three and six months post-operatively. Maturation rate at three months will be considered the primary endpoint with maturation rates at six weeks and six months and fistula volume flow and arterial and venous wall thicknesses at one and six weeks and three and six months considered secondary endpoints. At this time, the data will be analyzed to determine whether a cutoff VDI can be established which segregates patients into mature versus failure to mature groups. Chi-square analysis or Fisher's exact test will be used to compare the groups.

**Progress:** This protocol remains open to patient entry, with five patients enrolled during FY06. Data collection continues.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206116	<b>Status:</b> Ongoing
<b>Title:</b> Breast Papillomas in the Era of Stereotactic Core Biopsy		
<b>Principal Investigator:</b> CPT Vance Y. Sohn, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; CPT Joren B. Keylock, MC		
<b>Start - Completion:</b> 8/15/2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine natural history of breast papillomas diagnosed during core needle biopsy.

**Technical Approach:** This will be a retrospective chart review of all patients with a diagnosis of papilloma on core needle biopsy. Data will be further analyzed with follow-up radiographic and other clinical notes. Those patients who underwent excisional biopsy will be compared to those who did not undergo immediate biopsy, but were rather follow-up serially with radiographs.

**Progress:** From January 1994 until December 2005, 5,257 stereotactic core needle biopsies (SCNB) were performed at our tertiary level medical center; 206 patients were diagnosed with 215 breast papillomas; 172 (80%) papillomas were benign, 25 (12%) were associated with atypia, and 15 (7%) were associated with malignancy. Three benign papillomas (1.7%) developed into cancer (1 infiltrating ductal carcinoma, 2 ductal carcinoma in-situ) over an average of 44 months. Average follow-up of those patients not undergoing excision for benign papilloma was 41 months, although we had 92 patients with greater than 2 year follow-up and 57 patients with greater than 4 year follow-up. Of patients with atypia or malignancy associated with papilloma, there was a 26% and 87% associated rate of malignancy, respectively. This protocol remains ongoing for continued data analysis and completion of final paper.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206114	<b>Status:</b> Ongoing
<b>Title:</b> Institutional Accuracy of 11- and 8- Gauge Vacuum-Assisted Core Biopsy of Mammographic Breast Lesions		
<b>Principal Investigator:</b> CPT Vance Y. Sohn, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC		
<b>Start - Completion:</b> 8/8/2006 - Dec 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the accuracy of 11 and 8 gauge core needle stereotactic vacuum-assisted needle biopsy.

**Technical Approach:** A review of Breast pathway charts will be completed to identify patients with a diagnosis of atypical ductal hyperplasia on core biopsy who went on to open surgical biopsy. Of these, patients will be selected with a subsequent diagnosis of DCIS or invasive carcinoma and stratified according to the mammotome gauge. Correlation and analysis will be performed to see the accuracy of diagnosis of the 11 and 8 gauge mammotome between core needle biopsy and final excisional surgical biopsy. Results will be compared to published surgical literature.

**Progress:** The protocol remains ongoing for continued data analysis and completion of final paper.

From June 1996 until July 2006, 4,579 stereotactic core needle biopsies (SCNB) were performed at our tertiary level medical facility; 78 of 88 (89%) of patients diagnosed with ADH on SCNB with an 11-gauge vacuum-assisted needle underwent open surgical excision. Of these patients, nine (11%) were upgraded to ductal carcinoma in-situ (DCIS) while five (6%) had infiltrating ductal carcinoma (IDC) for a total underestimation rate of 17%. These results differ from our previously published series of 14-gauge SCNB which revealed an underestimation rate of 36%. Mean age of our patients was 58 years, with 71 (82%) undergoing percutaneous biopsy for microcalcifications discovered on routine mammography. Most common excisional diagnosis was focal ADH or atypical lobular hyperplasia (ALH) in 44 (56%) patients. Mean number of passes obtained at time of biopsy, mean age of patients, and characteristic radiographic abnormality were similar for malignant and benign diagnosis.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206004	<b>Status:</b> Ongoing
<b>Title:</b> The Evaluation of Telomerase Inhibition in a Colorectal Metastasis Model Using Nude Mice (Mus musculus)		
<b>Principal Investigator:</b> CPT Vance Y. Sohn, MC		
<b>Department:</b> Surgery/General Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Tommy A. Brown, MC; COL Kenneth S. Azarow, MC; CPT Jason T. Perry, MC; CPT Garth S. Herbert, MC		
<b>Start - Completion:</b> 11/8/2005 - Oct 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** This study will test imatinib mesylate in vivo to determine its efficacy in limiting metastatic spread of human colon cancer in nude mice.

### Technical Approach: Experiment 1

A pilot study will be conducted to validate the method of delivery of tumor cells. Mice will be anesthetized under standard policy as per the MAMC veterinarian. 26 mice will be used, 13 in each group. A mini-laparotomy will be performed and the spleen mobilized. Approximately 4 million colon cancer cells suspended in saline vs. saline alone will be injected into the subcapsular space of the spleen using a 26 gauge needle. After 10 minutes, the splenic vessels will be ligated, and the spleen removed. The abdominal incision will then be closed using simple interrupted sutures of 4.0 Vicryl. The animals will then be returned to their cages, which will be maintained at 90oF until animals have recovered fully from anesthesia. They will be allowed food and water ad lib. All mice will be observed for evidence of study endpoints. All surviving mice will be sacrificed at 60 days following surgery. The liver will be removed, and weighed in order to quantify the extent of metastatic spread. Data from mice who had saline alone injected into the spleen will be used establish a baseline liver weight. The percentage of mice surviving, as well as the length of time required for appreciable tumor growth may dictate modification of these factors in subsequent experiments.

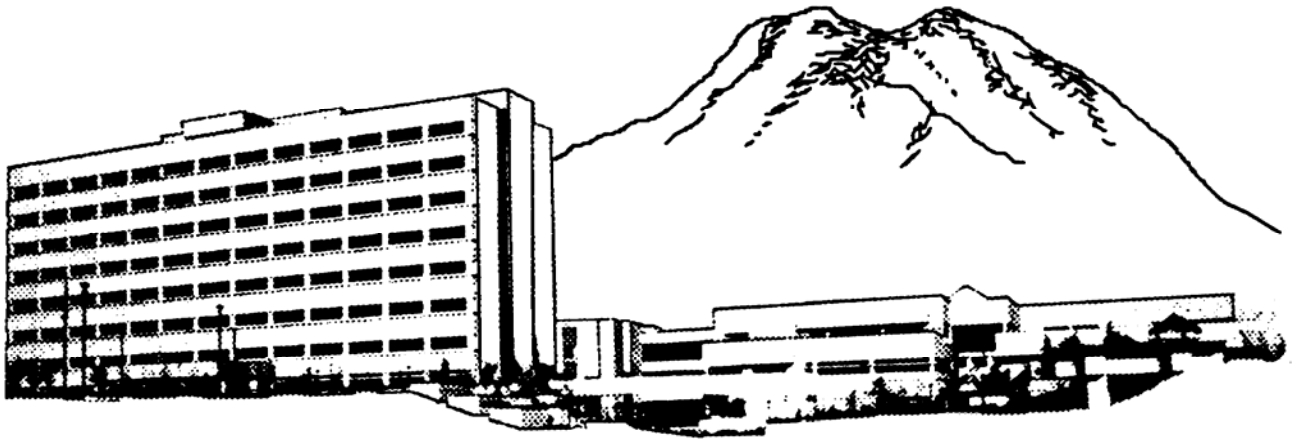
### Experiment 2

After verifying that the above model of tumor metastasis functions effectively, we will begin the second arm of the study. Mice will undergo the same procedure as detailed above. We intend on using 13 mice per group, although survival results and tumor size in Experiment 2 may require modifications. One half of the mice will then be administered imatinib mesylate (10mg/kg/day) orally (gavage), while mice in the control group will receive saline gavage. Again, the animals will be allowed food and water ad lib. All mice will be observed daily, watching for study endpoints as detailed in V.4.5. All surviving mice will be sacrificed at 60 days following surgery. The liver will be removed, and weighed in order to quantify the extent of metastatic spread. The mass of the liver will be compared between the two groups to quantify the ability of imatinib mesylate to inhibit metastatic spread of colon cancer. In addition, portions of the liver will also be frozen for subsequent quantification of telomerase activity.

### Experiment 3

Additional experiments using the model established above will be conducted using other telomerase inhibitors, as compared to imatinib mesylate, or in conjunction with established anti-neoplastic agents with efficacy against colon cancer, such as 5-fluorouracil, irinotecan, capecitabine and bevacizumab. Again, based on preliminary power analysis, 13 animals will be required per group (with approximately 8 groups to include a control group, an imatinib only group, and multiple groups that receive other antineoplastic agents with or without imatinib).

**Progress:** The plan was for a multi-armed procedure using mice. During the first pilot study, a power analysis was performed after completion as described in the original protocol in which the numbers required to proceed was greater than 40,000 mice. Therefore, a repeat pilot was performed. This too however was unsuccessful. We are currently reviewing the literature to determine the technical aspects to continue with this protocol.



## **Detail Summary Sheets**

Ophthalmology Service, Department of  
Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204085	<b>Status:</b> Completed
<b>Title:</b> Flow Cytometry Descriptive Findings from Lacrimal Sac Biopsy Specimens, Obtained in Standard Dacryocystorhinostomy		
<b>Principal Investigator:</b> LTC Darryl J. Ainbinder, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Jerome B. Myers, MC; CPT Travis C Frazier, MC; COL Robert A. Mazzoli, MC; CPT Kerry L. O'Brien, MC		
<b>Start - Completion:</b> 6/16/2004 - May 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/22/2005

**Study Objective:** This study will provide a descriptive baseline of the flow cytometry findings from lacrimal sac biopsy specimens obtained in standard dacryocystorhinostomy.

**Technical Approach:** Investigators will conduct a prospective descriptive study of the flow cytometric features, of tissue specimens obtained during standard dacryocystorhinostomy surgery, in adults. These tissue specimens currently receive standard histopathologic evaluation. The study plans to enroll a maximum of 50 patients from two staff oculoplastic surgeons who present to the Ophthalmology Service for symptoms of chronic dacryocystitis and adult nasolacrimal duct obstruction. On histopathology, the overwhelming tissue diagnosis is chronic inflammation of the lacrimal sac. Demographic data will be collected and clinical findings reported on standard oculoplastic history and physical examination sheet. Only one study provider will transfer the clinical data onto a numeric study database. Raw data and flow cytometry descriptive reports will be collected, as well as the histopathologic final tissue diagnosis. The data collection process will be numerically coded with no patient protected health or identifying information in the database. At the end of one year data collection will be discontinued. Investigators will review and present the flow cytometric features of patients undergoing standard dacryocystorhinostomy. The final tissue histopathology will allow correlation with flow cytometric findings to tissue histopathology. The demographic and clinical data will allow characterization of basic features of the study clinical population.

**Progress:** This protocol was reported completed in May 2006, with six patients enrolled in the last twelve months for a total enrollment of nine. The descriptive findings on flow cytometry demonstrated a consistent description of the sub mucosal chronic inflammatory infiltrate found on histopathology of standard patients undergoing dacryocystorhinostomy for nasolacrimal duct obstruction. Flow cytometry demonstrates a mixed population of phenotypically normal B and T cells. There has been no evidence of light chain restriction. These findings help to build a descriptive baseline of flow cytometry results in patients with obstruction who do not have confounding malignancy or granulomatous disease.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206076	<b>Status:</b> Completed
<b>Title:</b> Methicillin Resistant Ascending Facial and Orbital Cellulitis in Operation Iraqi Freedom Troop Population		
<b>Principal Investigator:</b> CPT John H. Boden, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Darryl J. Ainbinder, MC		
<b>Start - Completion:</b> 4/6/2006 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** (1) To present a descriptive case series of methicillin resistant ascending facial and orbital cellulitis in Operation Iraqi Freedom (OIF) troop population. (2) To make aware that methicillin resistance must be considered in rapidly progressive skin and soft tissue infections in active duty troop population. Occult, resistant, nasal infections may be the source for ascending orbital cellulitis.

**Technical Approach:** Physician will transfer summaries of patients cared for and treated by Col Ainbinder while serving in Operation Iraqi Freedom for review. Patients with MRSA facial cellulitis from a peri-nasal or nasal mucosal source will be evaluated. Of those, cases which demonstrated ascending progression to peri-orbital, or orbital cellulitis will be included in this review.

**Progress:** In a retrospective review of MRSA isolates obtained at an Army community hospital, the prevalence of MRSA isolates increased from 12% in 1998 to 43% in 2003. This study also demonstrated that over a five year period, 93% of MRSA isolates were cultured from out-patients without any risk factors for hospital-associated MRSA. This study presented five cases of aggressive ascending facial cellulitis with peri-orbital or orbital cellulitis from a nasal mucosal source. None of the cases had CT or clinical evidence of a sinus source of infection. It is important to note that in every case, the patient assumed that the small abscess inside the nares was not related to their illness. None of the patients complained of nasal pain until nasal inspection with a speculum was performed. Nasal cultures demonstrated MRSA and greatly assisted in the treatment of each patient. It is imperative that the treating physician be cognizant of the increasing prevalence of MRSA infections and be aware that a superficial nasal MRSA infection can progress to orbital cellulitis, meningitis, and possibly death. The nasal source can be occult due to the distracting presentation of the orbit and systemic findings. These patients look sick, and the proptotic globe changes are striking. It is imperative to examine, culture, drain wounds from the nose in patients presenting with peri-orbital or orbital cellulitis so that a nasal follicular abscess will not be overlooked.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206124	<b>Status:</b> Ongoing
<b>Title:</b> The use of lidocaine gel prior to povidone - iodine antisepsis and its effect on microbial survivability		
<b>Principal Investigator:</b> CPT John H. Boden, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Mark F. Torres, MC; CPT David M. Bushley, MC		
<b>Start - Completion:</b> 9/21/2006 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if the use of lidocaine gel prior to povidone-iodine antisepsis carries an increased risk of microbial survivability

**Technical Approach:** 1. A standard 0.5 McFarland suspension of *Staphylococcus epidermidis* will be diluted 1:10 with normal saline. A 0.001 ml loop will be used to inoculate each plate to give a standard  $1 \times 10^4$  to  $1 \times 10^5$  colony forming units on each blood agar plate.

2. A control group of 5 blood agar plates will be inoculated and labeled

3. A group of 5 plates of inoculated blood agar will have lidocaine gel applied to the plate. The lidocaine gel will be allowed to drip across the agar plate as the plate is held vertically. After the lidocaine gel has covered the entire plate, the excess lidocaine gel will be wiped out using a sterile cotton tip applicator, and the plate will be stored upside down so that residual lidocaine gel can continue to drop off the agar plate. Each plate will be labeled.

4. A group of 5 inoculated blood agar plates will have lidocaine gel applied to the plate in the same manner as step 3. The plate will be placed upside down to allow excess gel to drip off the plate for 5 minutes. Dilute povidone-iodine 5% ophthalmic solution will be placed onto agar plate so that it covers the plate. The povidone-iodine solution will be left in place for 30 seconds and then the residual povidone-iodine solution will be dumped out of the agar plate. Each plate will be labeled.

5. A group of 5 plates of inoculated blood agar will have dilute povidone-iodine 5% ophthalmic solution placed onto agar plate and allowed to cover the plate for 30 seconds. After 30 seconds the povidone-iodine solution will be dumped out of the agar plate. Each plate will be labeled.

6. Steps 1 through 5 will be repeated 3 more times, but instead of using *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Haemophilus influenzae* will be used in each reiteration respectively. When *Haemophilus influenzae* is used standard chocolate agar will be used instead of blood agar.

7. The plates will be placed in a standard microbiology incubator used for aerobic culture, and microbial growth will be evaluated 24 hours later. If there is no growth after 24 hours, the plates will be reevaluated after another 24 hour time

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee, effective 20 September 2006.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206006	<b>Status:</b> Ongoing
<b>Title:</b> Virtual Ophthalmosurgical Simulator as a Valid Training Tool		
<b>Principal Investigator:</b> CPT Daniel J. Solverson, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Robert A. Mazzoli, MC; LTC William R. Raymond IV, MC; LTC Mark L. Nelson, MC; COL Kenneth S. Azarow, MC; COL Craig D. Hartranft, MC		
<b>Start - Completion:</b> 10/21/2005 - Feb 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** To establish the validity of an ophthalmosurgical virtual reality simulator for intraocular surgery as an educational and assessment apparatus.

**Technical Approach:** All medical students, residents, ophthalmology staff physicians willing to participate will be recruited, have a visual acuity exam and be asked to complete a questionnaire to assess level of experience regarding microsurgery and handedness. All subjects will receive specific instructions on how to perform a navigation task on the EYESI virtual reality simulator by watching an instructional videotape. Each participant will complete several tasks including arranging small spheres near the retina and peeling a membrane off the retina. Main outcome measures in the arrangement task will be time to complete task as well as time to first error (such as a retinal hit) and participant microtremor throughout task. Each participant will also consecutively perform each task for a total of 15 times. Time intervals will be recorded between each consecutive task. Evaluations include: the relationship between the surgical experience and the task's completing time using ANOVA; the relationship between stereopsis and the task's completion time using Pearson correlation test; and the relationship between the surgical experience and the average tremor score using Pearson correlation test. To study the learning curve, the consecutive completion times for each subject and ANOVA will be evaluated to determine if there was a significant decrease in completion time throughout the 15 trials. For the membrane peeling task, the relationship between surgical experience and stereopsis with the number of retinal contacts, the task's completion time, and average tremor using ANOVA or Pearson correlation test will be evaluated, as appropriate.

**Progress:** This protocol remains open to enrollment, with 35 subjects entered who have undergone the testing on the virtual reality simulator. Comparing expert and novice surgeon performance on same task, preliminary data shows that expert surgeons showed a greater facility with microsurgical tasks, but with repeated practice, novice surgeons showed improvement in all performance scores.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204049	<b>Status:</b> Completed
<b>Title:</b> Long-Term Follow-up of Military Personnel Following Photorefractive Keratectomy With Mitomycin-C		
<b>Principal Investigator:</b> LTC Mark F. Torres, MC		
<b>Department:</b> Surgery/Ophthalmology Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Roger A. Anderson, MC; CPT Steven J. Rogers, MC; CPT Adam G. Buchanan, MC		
<b>Start - Completion:</b> 3/17/2004 - Mar 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 3/22/2005

**Study Objective:** (1) To determine the effect of mitomycin-c on post-operative refraction when it is used in Photorefractive Keratectomy (PRK). (2) To assess for the presence of corneal haze following Photorefractive Keratectomy with mitomycin-c.

**Technical Approach:** A retrospective chart review will be conducted on all subjects who have undergone Photorefractive Keratectomy with Mitomycin-c at the Madigan Refractive Surgery Center. The study will include approximately 20-30 subjects in the 18-50 year old age range. The final number of subjects will depend on how many meet entry criteria at the time the study is initiated. For each chart reviewed data will be recorded on subject's pre-operative and postoperative vision and refraction (spectacle prescription) and comparing the actual results (paired t-test) to the predicted values. The presence or absence of postoperative corneal haze, wound recidivism, will also be assessed. A protocol revision expanded the chart review to include all patients undergoing PRK with adjunctive use of mitomycin C through Jan 05. The number of charts planned to reviewed was updated to 30 to 50.

**Progress:** Although an amendment to the protocol was approved in April 2005, no study activity occurred during that fiscal year or in fiscal year 2006. This study is completed at MAMC.

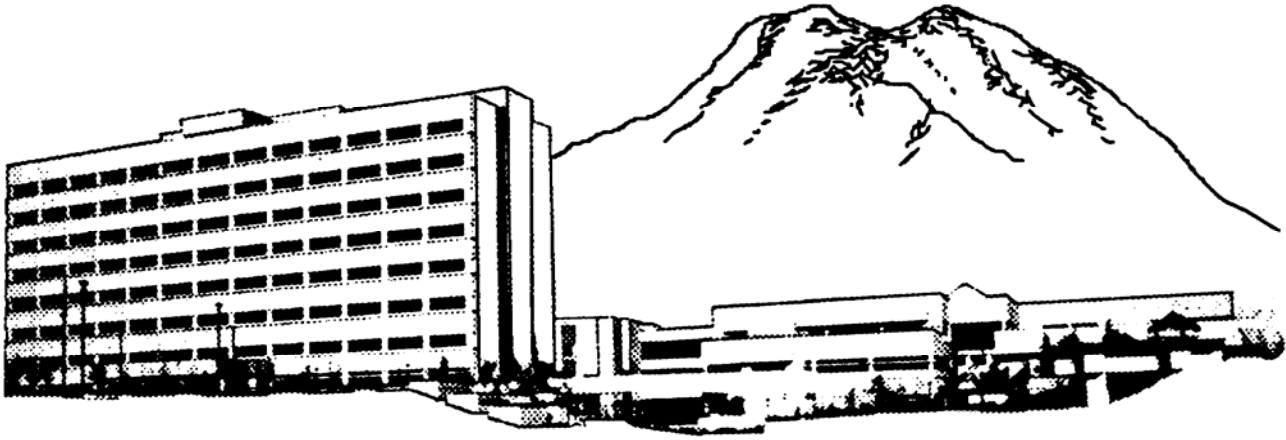
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 205083	<b>Status:</b> Ongoing
<b>Title:</b> Ophthalmic Phentolamine Multiple Dose Clinical Trial			
<b>Principal Investigator:</b> LTC Mark F. Torres, MC			
<b>Department:</b> Surgery/Ophthalmology Surgery			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Aaron G. Amacher, MC			
<b>Start - Completion:</b> 11/17/2005 - Apr 2005		<b>Funding:</b> Ocularis Pharma via The Geneva Foundation	<b>Periodic Review:</b> 6/7/2006

**Study Objective:** Determine the effect on pupillary diameter of multiple doses of ophthalmic phentolamine (OP). Determine the effect on contrast sensitivity, glare sensitivity, and visual acuity of multiple doses of (OP). Determine the subjective benefits of multiple doses of OP. Determine the onset of action, the time of peak effect and the duration of the response of OP following multiple doses. Determine the safety and tolerability of OP following multiple doses.

**Technical Approach:** The Ophthalmic Phentolamine (OP) Multiple Dose Clinical Trial will study 12 otherwise healthy, 21-55 year old men and women who have had refractive surgery and have post surgical complaints of night vision problems. The study will be a randomized double-blinded placebo controlled crossover study with two periods. Each patient will receive two of three possible treatments: placebo, 0.2%, or 0.4% phentolamine. Pupil size, contrast sensitivity, glare sensitivity, accommodation, blood pressure and heart rate will be measured prior to application of OP. Following OP administration these variables will again be measured at intervals of one, four, and eight hours. Pre- and post-OP administered pupillary size, contrast sensitivity, visual acuity, glare sensitivity, subjective assessments, blood pressures and heart rates will be statistically compared in order to: (1) Determine the effect on pupillary diameter of multiple doses of ophthalmic phentolamine (OP). (2) Determine the effect on contrast sensitivity, glare sensitivity, and visual acuity of multiple doses of (OP). (3) Determine the subjective benefits of multiple doses of OP. (4) Determine the onset of action, the time of peak effect and the duration of the response of OP following multiple doses. (5) Determine the safety and tolerability of OP following multiple doses.

**Progress:** This protocol remains open to enrollment, but no glare patients have yet been identified. Recruitment continues.



## Detail Summary Sheets

Orthopedics Service, Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206022	<b>Status:</b> Ongoing
<b>Title:</b> Accuracy of Reduction Utilizing Volar Fixation for Dorsally Displaced Fractures of the Distal Radius		
<b>Principal Investigator:</b> CPT Ivan J. Antosh, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Joshua P. Herzog, MC; COL Sean D. Ghidella, MC; LTC John G. DeVine, MC; CPT Llewellyn V. Lee, MC		
<b>Start - Completion:</b> 2/8/2006 - Nov 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/26/2006

**Study Objective:** To determine the accuracy of a volar fixed angle plate in operatively treated distal radius fractures.

**Technical Approach:** This study will enroll the next 34 patients that present with a distal radius fracture who are selected by the treating physician to undergo surgical correction with a Hand Innovations DVR plate. All patients will undergo a preoperative and postoperative CT scan of their wrist. There will be no change in the operative approach, surgical technique or postoperative rehabilitation. Demographic and contact information will be gathered.

Radiographic measurements of the injury CT and post-op CT will be evaluated by three separate readers and the averages used for statistical calculations. The films will be evaluated for (1) radial height, (2) radial inclination (3) dorsal/volar angulation (4) articular step-off (5) articular gapping (6) degree of comminution using a visual analog scale, (7) presence or absence of distal radioulnar joint (DRUJ). The preoperative measurements will then be compared to the postoperative measurements utilizing the paired student T-test. The data from this study will be used to predict the accuracy of reduction with utilization of the Hand Innovations DVR plate.

**Progress:** Due to scheduling and time constraints, no patients were enrolled during FY06. Investigators plan to begin subject enrollment in November 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206037	<b>Status:</b> Ongoing
<b>Title:</b> A Retrospective Review of Injuries Sustained During Operation Iraq Freedom and Operation Enduring Freedom Requiring Medical Evacuation to a Tertiary Medical Center		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Joshua P. Herzog, MC; CPT John A. Guzzo, MC; LTC John G. DeVine, MC		
<b>Start - Completion:</b> 12/21/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/8/2006

**Study Objective:** To provide an expanded casualty survey of evacuations to an Army Medical Center over the past 22 months via a retrospective chart review.

**Technical Approach:** Utilizing the daily OIF/OEF patient diagnosis report from Jan 2003-Nov 2005 approximately 1085 soldier who were evacuated from OIF/OEF have been identified. A retrospective chart review using CIS, ICDB, ORMA and Dinpacs will be conducted. Demographic data to include age, sex, MOS and military rank will be collected. The patient diagnosis report and the detailed chart review will be used to document the type of injuries (Fracture, Neuro/vascular Damage, Amputation, Wound Care, Overuse Syndromes, Ligament Damage), Location of Injuries (Hand, Forearm, Arm, Shoulder, Foot, Leg/Ankle, Femur, Hip, Pelvis, Spine), Disease Non-Battle Injury vs. Combat Injury, Treatments, Number of days from injury, Pre-existing condition. Army Personnel Command will also be contacted to determine the normal demographical data for deploying soldiers out of the Pacific Northwest. This data will then be compared to the med-evac patient population to evaluate for a statistical difference. The data will be further evaluated by graphical means.

**Progress:** This is a retrospective review of patients with injuries sustained during Operation Iraq Freedom (OIF) and Operation Enduring Freedom (OEF) who required medical evacuation to Madigan Army Medical Center. Data collection was completed during FY06; data analysis had begun.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201015	<b>Status:</b> Ongoing
<b>Title:</b> Biomechanics of Various Coracoclavicular Ligament Reconstruction Techniques		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Kurtis L. Kowalski, MC; COL (Ret) Patrick St Pierre, MD; CPT Brendon R. Connolly, MC; MAJ Paul M. Ryan, MC; MAJ Creighton C. Tubb, MC; CPT Wendy J. Boucher, MC; CPT Joshua P. Herzog, MC		
<b>Start - Completion:</b> 11/15/2000 - Dec 2004	<b>Funding:</b> Mitek via Proffer	<b>Periodic Review:</b> 9/21/2006

**Study Objective:** Test the strength and biomechanical characteristics of native and intact coracoclavicular ligament complexes as well as various reconstructive techniques for treating high-grade acromioclavicular joint separations.

**Technical Approach:** Thirty coracoclavicular bone-ligament-bone specimens will be harvested from fresh-frozen human cadavers. Unidirectional tensile loading will be performed with the Instron device. Tensile loading will be applied to the clavicle at a uniform rate until failure of the coracoclavicular ligament complex occurs. The coracoclavicular ligament will then be reconstructed using gracilis tendon, palmaris longus tendon, or SIS graft. The grafts will be looped multiple times under the coracoid process and over the top of the clavicle. It will be secured to itself with a #2 Ethibond suture. They will then be tested to failure as previously described.

Data will be obtained from the Instron device regarding tensile strength, load to failure, stiffness, and elongation to failure. Statistical analysis will be performed using a one-way ANOVA to determine differences between groups as well as Duncan's multiple range test to determine specific differences.

**Progress:** This bench protocol remains ongoing. Since initiation, numerous cadaver matched shoulders have been tested, both controls and experimentals. The data appears to be good and reproducible. Statistical analysis continues to determine what the next step needs to be, including the testing of additional matched controls and refinement of Instron techniques. Investigators have also begun testing additional experimental reconstructions.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204051	<b>Status:</b> Ongoing
<b>Title:</b> Efficacy of Post-operative Hip Spica Wrap Dressing after Primary Hip Arthroplasty in Preventing Post-operative Wound Complications and Blood Transfusions		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Aaron H. Hoblet, MC; MAJ James A. Hall, MC; CPT John J. McGuigan, MC; CPT Nathan T Boykin, MC		
<b>Start - Completion:</b> 9/8/2004 - July 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2/22/2006

**Study Objective:** To determine the efficacy of post-operative hip spica wrap dressing in primary hip arthroplasty in preventing wound complications and blood transfusions.

**Technical Approach:** Patients undergoing total hip arthroplasty or hemi-arthroplasty, electively or due to trauma, over the age of 18, male or female, are eligible to participate in this study. The next 20 patients who meet inclusion criteria will be randomly selected, after wound closure, to be placed in group A (standard wound closure with standard dressing and paper tape plus a hip spica wrap dressing) or Group B (the control group, standard wound closure with standard dressing of perforated cloth tape without the hip spica wound dressing). Data will be recorded pre-operatively to include medical comorbidities, height, weight, pre-albumin, albumin, hematocrit and post-operatively to include length of incision, amount of drainage per dressing, weight, the change in hematocrit, the need for a transfusion, length of hospital stay and any wound complications. Using the Student's T-test, this study will show a statistically significant decrease in wound drainage, decreased number of wound complications, decrease in length of hospital stay, smaller drop in the hematocrit and decrease need for transfusions.

**Progress:** This protocol has not been initiated awaiting an orthopaedic research coordinator to facilitate data collection and a total joint surgeon to be in place to enroll potential subjects.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203036	<b>Status:</b> Ongoing
<b>Title:</b> Intramedullary Fixation of Displaced Acute Middle One-Third Clavicle Fractures		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Karin A. Johnson, MC; CPT John J. McGuigan, MC; Steven D. Travers, MPT; LTC Craig R. Bottoni, MC; MAJ Eric L. Smith, MC		
<b>Start - Completion:</b> 3/18/2003 - Mar 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** To determine the usefulness of intramedullary fixation of the treatment of 100% displaced middle one-third clavicle fractures. Compare the rates of union, nonunion, and malunion versus non-operative treatment.

**Technical Approach:** This study will randomize patients with acute displaced middle one-third clavicle fractures to either standard non-operative treatment or to open reduction and intramedullary pin fixation. The ultimate goal of this research is to obtain fracture healing with anatomic alignment, in order to promote an earlier return to full duty using a minimally invasive method of fracture stabilization. If successful, normal shoulder mobility and function will be restored faster and the patients can return to full activities sooner.

**Progress:** This protocol continues to actively recruit subjects. Since initiation, fifteen subjects have enrolled, six during FY06. No complications or adverse events have occurred.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206085	<b>Status:</b> Ongoing
<b>Title:</b> Pectoralis Major Repairs in Active Duty Soldiers		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jason A. Grassbaugh, MC; CPT Ivan J. Antosh, MC; LTC John G. DeVine, MC		
<b>Start - Completion:</b> 5/8/2006 - Mar 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** A retrospective review of all pectoralis major repairs performed at Madigan Army Medical Center from 2000 to 2006 with an objective to define expected results in terms of strength, functionality, pain, and ability to return to work among the active duty population.

**Technical Approach:** A list of all active duty soldiers who underwent operative repair of pectoralis major tendon tears from 2000-2006 will be gathered from operative records. Chart review will be performed in order to ascertain date of surgery, operative findings, repair methodology, rehabilitative plan and follow up visitations. After obtaining this data, patients will be contacted in writing in order to complete the DASH (Disability in arm, shoulder, and hand questionnaire). Results will be accumulated and analyzed.

**Progress:** This is a retrospective review of the functional outcome of pectoralis major rupture repairs in active duty Soldiers. Fifteen patients treated over the past four years at MAMC have been contacted during FY06. Information has been returned from thirteen patients. The protocol remains ongoing to conduct data analysis.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206036	<b>Status:</b> Ongoing
<b>Title:</b> Return to Full Duty after Anterior Cruciate Ligament Reconstruction in the Military Population		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC John G. DeVine, MC; CPT Joshua P. Herzog, MC		
<b>Start - Completion:</b> 12/20/2005 - Jun 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/8/2006

**Study Objective:** Objectives are to determine the rate of return to a soldier's pre-injury MOS after undergoing an anterior cruciate ligament (ACL) reconstruction and to identify risk factors to assist in predicting a decrease rate of return to full duty.

**Technical Approach:** A retrospective chart review of all 604 active duty patients who underwent an ACL reconstruction from 1994-2002 will be performed to identify potential predictors of poor outcomes, such as Age, Gender, MOS, time from injury to surgery, graft choice, intra-articular injuries (meniscal tear, meniscal treatment, chondral injuries, chondral treatment), duration of follow-up. Patients will be mailed questionnaires that will include four validated outcome instruments, a review of systems, questions regarding additional surgery, questions regarding any changes in social or demographic information. Patients will be asked what their pre-injury MOS was and if this was maintained post-rehabilitation (6 months); their current occupation; if they have ever undergone an MEB and the underlying condition that generated the MEB, and if they have a permanent profile for symptoms related to the operative knee. The primary outcome is the presence of an MEB, MOS change or Perm Profile as a result of symptoms related to the operative knee. This study will demonstrate the attrition rate in active duty soldiers after and ACL reconstruction and serve to identify predictors via a statistical model to predict who fails active duty ACL reconstructions.

**Progress:** This is a retrospective mailed review of functional outcome after ACL reconstruction. No patients were contacted during FY06; a useable database with current contact information has not been identified.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200065	<b>Status:</b> Completed
<b>Title:</b> Study of the Treatment of Articular Repair (STAR): A Prospective, Longitudinal Within Patient Evaluation of the Effectiveness (Durability) of Carticel (autologous cultured chondrocytes) Compared to Non-Carticel Surgical Treatment for Articular Cartilage Defects of the Knee		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ James A. Hall, MC; LTC Doug A. Vermillion, MC; COL (Ret) Patrick St Pierre, MD		
<b>Start - Completion:</b> 6/29/2000 - Jun 2006	<b>Funding:</b> Genzyme via Henry M. Jackson Foundation	<b>Periodic Review:</b> 3/21/2006

**Study Objective:** To compare the effectiveness (durability) of Carticel autologous chondrocyte implantation in patients who have had an inadequate response to a prior non-Carticel surgical cartilage repair procedure (including debridement, microfracture, drilling, abrasion arthroplasty or other surgical treatment) within the previous 3 years for significant articular cartilage defects of the femoral condyle.

**Technical Approach:** This study will be a longitudinal, prospective, multicenter, within patient evaluation of 100 patients with articular cartilage defects of the knee who have had inadequate response to a prior non-Carticel surgical treatment. Patients who had an inadequate response to a prior non-Carticel surgical treatment will be implanted with Carticel (autologous cultured chondrocytes). The overall condition of the knee will be evaluated Using Modified Cincinnati Knee Rating System at baseline and every 6 months postoperatively. The SF-36 health survey will be used to assess global health status at baseline and follow-up visits. The primary endpoint of the study will be time to treatment failure, and will be compared via chart review of consented patients to the durability of past treatments.

**Progress:** This protocol closed to patient enrollment in June 2001, with five subjects enrolled at MAMC. All subjects received study treatment and four completed scheduled follow-up visits. One subject was reported to the study sponsor and the IRB as lost to follow-up. A study site closure visit was conducted 18 April 2006. Three internal serious adverse events were reported and assessed as possible causality with study participation. There were no unreported serious adverse events at the time of this report.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200125	<b>Status:</b> Ongoing
<b>Title:</b> Subacromial Injection of Corticosteroids versus Ketoralac for Treatment of Shoulder Impingement Syndrome		
<b>Principal Investigator:</b> COL Edward D. Arrington, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Paul M. Ryan, MC; MAJ Bryant G. Marchant, MC; CPT Neil C. Vining, MC; COL (Ret) Patrick St Pierre, MD; MAJ Christopher J. Wilson, MC; CPT Brian K. Konowalchuk, MC		
<b>Start - Completion:</b> 9/5/2000 - Jun 2001	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/23/2005
<b>Study Objective:</b> To evaluate the difference in pain relief and functional outcome for subacromial impingement syndrome for patients who are treated with either a subacromial injection of corticosteroids or a subacromial injection of Ketoralac.		
<b>Technical Approach:</b> This double-blind, randomized study will enroll approximately 40 patients with uncomplicated impingement syndrome for treatment with either subacromial corticosteroids or Ketoralac. Subjects with subacromial impingement will be given either 6cc 1% lidocaine with epinephrine and 40 mg Triamcinolone (Control) or 6cc 1% lidocaine with epinephrine and 60mg injectable Toradol (Test). Patient evaluation will be done at the time of injection and at 4 weeks post-injection.		
<b>Progress:</b> This study closed to patient entry with 48 patients enrolled; 6 during FY06. The protocol remains ongoing for data analysis. There were no adverse effects that occurred during this study.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205300	<b>Status:</b> Ongoing
<b>Title:</b> Stryker Biotech- OP-1 Bone Morphogenetic Protein, BMP-7 (HUD)		
<b>Principal Investigator:</b> LTC Paul L. Benfanti, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Edward D. Arrington, MC; LTC John G. DeVine, MC; COL Sean D. Ghidella, MC; MAJ James A. Hall, MC; CPT Glenn J. Kerr, MC		
<b>Start - Completion:</b> 3/8/2005 - Indef	<b>Funding:</b> Stryker via HDE	<b>Periodic Review:</b> 2/28/2006

**Study Objective:** Humanitarian Use Device

**Technical Approach:** OP-1 Bone Morphogenetic Protein will be used in patients that present with challenging and difficult to treat injuries that have a very poor success rate using normal methods and techniques. OP-1 represents the state of the art treatment of injuries that have challenged surgeons for decades, The success of this product lies in its use of a naturally occurring substance found in the human body to aid in the initiation of the natural cascade of events that promote bone healing. The incidence of adverse reactions associated with the implantation is less than 0.1%.

**Progress:** An audit was conducted in March 2006 following the report of three patients who received treatment with OP-1. At that time, the IRB placed oversight of all Humanitarian Use Devices on the Chief, DCI and DCI Auditor. No adverse effects were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205053	<b>Status:</b> Ongoing
<b>Title:</b> A Prospective, Randomized Clinical Investigation of the Cervitech, Inc. Porous Coated Motion Artificial Disc for Stabilization of the Cervical Spine at One Level between C3-C4 and C7-T1		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC John I. Iskandar, MC; COL Edward D. Arrington, MC; LTC Paul L. Benfanti, MC; MAJ Donny M. Melton, MC		
<b>Start - Completion:</b> 5/31/2005 - Feb 2012	<b>Funding:</b> Cervitech via Geneva	<b>Periodic Review:</b> 2/28/2006

**Study Objective:** The objective of this clinical study is to evaluate the safety and effectiveness of the PCM Porous Coated Motion Artificial Disc for treatment of degenerative disc disease compared to conventional ACDF in patients with DDD and neurological symptoms at one level between C3-C4 and C7-T1.

**Technical Approach:** This study plans to enroll 744 patients from areas across the US. Half of the patients will have surgery to remove the damaged disc and replace it with the study device (PCM). The other half of the patients will receive the current standard treatment; surgery to remove the damaged disc and then have the vertebrae fused together. This study will compare outcomes of disc surgery using the PCM Artificial Disc and the fusion surgery. Prior to surgery patients will have a physical exam, including x-rays, neurological testing, and either a MRI or CT scan (unless done in the past 12 months). A bone mineral density scan may be required to determine bone quality. The patient will also be asked to fill out surveys about neck symptoms, level of pain, and overall health. Patients will then be assigned to receive either the PCM or fusion procedure. The patients will not know which treatment they received until after surgery. Patients will be asked to return to the doctor's office for post-operative follow-up exams at 2-3 weeks, 6 weeks, 3 months, 6 months, 12 months, 24 months, and yearly thereafter until the study is completed, which may be 7 years after surgery. X-rays and patient surveys will be completed at these visits.

**Progress:** This protocol remains open to enrollment with 23 patients enrolled at MAMC; 16 during FY06, all completed the c-spine surgery. One adverse event was reported for a patient with an extra day hospital stay due to post-op nausea who recovered and is continuing with the study. Subjects are followed through serial follow-up appointments.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206120	<b>Status:</b> Ongoing
<b>Title:</b> A Single Blind, Multi-Center, Randomized, Prospective Clinical Study Comparing Optecure™ Autograft Extender to Autograft Only in Fusion of the Lumbar Spine		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Edward D. Arrington, MC; LTC Paul L. Benfanti, MC; MAJ Mark W. Manoso, MC; COL Sean D. Ghidella, MC; MAJ Eric M Bluman, MC		
<b>Start - Completion:</b> 12/7/2006 - Feb 2009	<b>Funding:</b> Exactech, Inc. via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective of this study is to provide radiographic evidence that Optecure™ DBM, when used as an autograft extender, produces successful fusion in the lumbar spine. Secondary objectives include, but are not limited to, evaluating potential differences between the treatment groups in the occurrence of successful fusion, Oswestry Disability Index scores, SF-12 scores, and perceived pain as measured by Visual Analog Scales (VAS).

**Technical Approach:** Consecutive patients, at multiple centers, who are to be treated with lumbar fusion of 1 or 2 segments (i.e. 2 or 3 consecutive vertebrae) between L2 and S1, will be screened for participation in this clinical study. Following informed consent, approximately 150 subjects will be enrolled at multiple sites with 75 subjects expected to receive the treatment material (Optecure™ with autograft) and 75 the control material (autograft). Randomization will be accomplished at a 1:1 ratio (treatment vs. control). Investigators will remain blinded to the treatment type until decortication of the primary surgical site is complete. At that time the Randomization Envelope for the specific subject will be opened and will contain the Randomization Worksheet denoting the treatment to be used. The subjects will remain blinded to the type of treatment they receive until their participation in the study is complete (i.e., all follow-up visits are complete, subject is terminated from the study, or subject withdraws from the study). The vendor representative will bring the product to the OR for each case. Both the study material (Optecure) and the control material (autograft) are currently in use at Madigan Army Medical Center for spinal fusion. Follow-up will continue for 2 years following surgery. Radiographic, functional, patient health and pain data will be statistically compared between the two groups. A single, blinded radiologist will analyze fusion success at 6 months, 1 year, and 2 years postoperatively.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 22 August 2006.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206081	<b>Status:</b> Ongoing
<b>Title:</b> Magnetic resonance imaging evaluation of adjacent segments after lumbar disc arthroplasty using the SB Charite implant		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Ivan J. Antosh, MC; CPT Brian J Woebkenberg, MC; LTC Stephen M. Yoest, MC		
<b>Start - Completion:</b> 4/24/2006 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine whether or not magnetic resonance imaging is a viable imaging modality to evaluate adjacent segment after lumbar total disc replacement surgery using the SB Charite implant.

**Technical Approach:** Patients consented will have an MRI scan of their spine during a follow-up clinic visit, which will be evaluated by a radiologist as well as a member of the study staff. Meaningfulness of the scan will be determined by evaluating the ability to visualize the superior and inferior endplates as well as the disc space at both the superior and inferior adjacent levels.

**Progress:** This protocol remains open to patient entry, with three patients enrolled out of five potential candidates. One patient has completed the post-operative MRI; two patients are waiting for MRI dates. One potential candidate has been lost to follow-up and could not be contacted; another patient refused study participation.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206082	<b>Status:</b> Ongoing
<b>Title:</b> Magnetic Resonance Imaging Evaluation of Adjacent Segments After Cervical Disc Arthroplasty Using the PCM Implant		
<b>Principal Investigator:</b> LTC John G. DeVine, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Ivan J. Antosh, MC; CPT Brian J Woebkenberg, MC; LTC Stephen M. Yoest, MC		
<b>Start - Completion:</b> 4/24/2006 - May 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine whether or not magnetic resonance imaging is a viable imaging modality to evaluate adjacent segment after lumbar total disc replacement surgery using the SB Charite implant.

**Technical Approach:** Patients consented will have an MRI scan of their spine during a follow-up clinic visit, which will be evaluated by a radiologist as well as a member of the study staff. Meaningfulness of the scan will be determined by evaluating the ability to visualize the superior and inferior endplates as well as the disc space at both the superior and inferior adjacent levels.

**Progress:** This protocol is open to patient entry, with five patients enrolled out of eight potential candidates for the study. Two patients have received their MRIs, three MRIs are pending. Two candidates were lost to follow-up and could not be contacted. Recruitment of the final patient continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205054	<b>Status:</b> Completed
<b>Title:</b> A Phase 2, Double-Blind, Randomized, Placebo-Controlled, Dose-Ranging Study to Evaluate the Efficacy and Safety of Three Doses of TAK-128 in Subjects with Mild to Moderate Diabetic Peripheral Neuropathy		
<b>Principal Investigator:</b> Vickie R. Driver, DPM		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Jay C. Erickson, MC; COL Curtis J. Hobbs, MC; COL (Ret) Charles A. Andersen, MD; Gary P. Degen, DPM; CPT John P. Ney, MC		
<b>Start - Completion:</b> 5/31/2005 - Mar 2006	<b>Funding:</b> Takeda via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objectives of this study are: (1) To determine whether TAK-128 can significantly improve or slow the rate of progression of diabetic peripheral neuropathy as measured by nerve conduction velocity. (2) To determine the safety of daily oral doses of TAK-128. (3) To compare the effects across three doses of TAK-128. Secondary objectives of this study are to evaluate the effects of TAK-128 on a series of validated clinical measures of neuropathy including: (1) Quantitative sensory testing (QST), (2) Symptoms and deficits, (3) Quality of Life measures. The primary variable is the change at 6 months from baseline for composite measure of maximal nerve conduction velocity. The nerves included in the composite will be the peroneal motor nerve, median motor nerve, median sensory nerve, and the sural sensory nerve.

The secondary variables are: (1) The change from baseline in vibration perception threshold measurements. (2) The change in pain scores as assessed by Short-Form McGill Pain Questionnaire (SF-MPQ). (3) The change in the neurological examination as measured by the Clinical Neurologic Examination (CNE). (4) The change in the electrophysiologic parameters for individual nerves, including amplitudes (5) The change in quality of life index as assessed by the SF-36 Health Survey.

The safety variables include: (1) Adverse events. (2) Clinical laboratory assessments (hematology, clinical chemistry, urinalysis, HbA1c). (3) ECG results. (4) Vital signs. (5) Physical examinations.

**Technical Approach:** The study population will comprise approximately 320 male and female subjects aged 18 to 70, inclusive, considered eligible on the basis of inclusion and exclusion criteria. Subjects will be randomized in a 1:1:1:1 ratio to 1 of 4 treatment regimens. The total duration of the study will be approximately 7.25 months and will consist of a Screening Period, Baseline/Randomization (Day 1), and Treatment Period for up to 6 months, and a follow-up visit 1 week post-treatment. During Screening (Day -21 to Day -1), the eligibility of the subjects will be assessed. Prior to Randomization, the site staff must confirm that subjects qualify based on the Inclusion/Exclusion Criteria (see Sections 6.2 and 6.3). Subjects will be randomized to TAK-128 10 mg (two 5 mg tablets QD), TAK-128 50 mg (two 25 mg tablets QD), TAK-128 100 mg (two 50 mg tablets QD) or placebo. At each visit, subjects will return all unused study medication and have all required study procedures performed. Study procedures should occur between 6:00 AM and 11:00 AM. Subjects should fast and must not take their daily dose of study medication prior to all visits. Adverse event (AE) monitoring and concomitant medication use will be reviewed. New study medication will be dispensed to the subject at all visits except for Weeks 1 and 2 and the Final Visit (Month 6) or Early Termination Visits.

**Progress:** This protocol was reported closed at MAMC in November 2005, with no subjects screened or enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 204098	<b>Status:</b> Terminated
<b>Title:</b> Cost of Treating Diabetic Foot Ulcers - At Madigan Army Medical Center			
<b>Principal Investigator:</b> Vickie R. Driver, DPM			
<b>Department:</b> Surgery/Orthopedic Surgery			<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Mary L. Byers, RN			
<b>Start - Completion:</b> 8/26/2004 - Feb 2005	<b>Funding:</b> Ethicon, Johnson & Johnson via The Geneva Foundation		<b>Periodic Review:</b> 7/1/2005

**Study Objective:** PRIMARY: (1) Determine the yearly institutional cost of treating Diabetic Foot Ulcers (DFU) at MAMC with advanced and standard care modalities based on a 5-year retrospective cohort analysis. SECONDARY: (1) Determine rates and predictors of limb preservation measures. (2) Characterize the effect of 'Advanced Care' (AC) on: "Incidence of recurrence and infection in existing DFUs," "Incidence amputations," and "Incidence of DFUs." (3) Identify predictors of amputations. (4) Create a novel detailed database of clinical outcomes, utilization, and cost in this cohort by incorporating retrospective chart abstraction with the linkage of existing clinical and billing. (5) Create a Markov Model of disease progression, including diabetic wound healing, in patients with Diabetes Mellitus (DM). (6) Calculate the cost effectiveness of advanced care modalities.

**Technical Approach:** This is a five-year retrospective cohort study of patients with DM who were seen at Madigan Army Medical Center (MAMC). Patients will be identified in an electronic claims database using ICD-9 codes for diabetes, diabetic wounds, associated procedures, and complicating illnesses. Individual claims will then be grouped into cost-driving events using certain assumptions regarding care based on published literature and investigator knowledge of current treatment practices in the MAMC system along with data gathered from patient records. After enrollment into the cohort, all healthcare events will be abstracted directly from the patients' charts into a relational database which links clinical events to existing claim-based and clinical databases. Costs will be calculated based upon MAMC institutional cost, as well as Medicare cost of events. The impact of advanced care modalities on rates of amputation, wound incidence and recurrence, and infection will be analyzed.

Results will characterize aggregate institutional costs of treatment by site of care (inpatient, hospital outpatient, pharmacy, home health, etc.) and will also include per-patient and per-disease event costs. Using existing claims-based methodology for classifying chronic episodes and measuring co-morbidity, sub-analyses may be performed. Additionally, sub-group analyses will be conducted on patients who receive certain specified DFU therapies. These results are intended to describe the institutional costs associated with the care of diabetes and diabetic wounds under various care modalities. The detailed data this cohort study will provide allows the identification of individual ulcer events, and can distinguish recurrences from novel ulcers. The effect of advanced care on the incidence of recurrence, as well as infection, amputation and death can be calculated as well. The cost-effectiveness of advanced care in terms of amputation-free years, as well as the number needed to treat (NNT) for advanced care, will be calculated. Costs will be obtained from the outcomes research department at the MAMC and from published Medicare data.

A Markov Model that characterizes diabetic, and chronic wound states will be used to analyze effectiveness of various approaches to wound care and disease management. Prediction of long-term outcomes, and cost-effectiveness analysis based upon the Markov Model output will be carried out.

**Progress:** This protocol was officially terminated for cause by the MAMC IRB, 26 September 2006. During the conduct of this retrospective review protocol, Dr. Driver failed to (1) seek HUC approval for study personnel given access to approximately 550 MAMC subjects' medical records, (2) maintain the privacy of MAMC subjects' PHI by sending e-mail operative reports to a non-MAMC employee who was not recognized by the HUC as a member of the study staff, (3) submit CVs and proof of human subjects training for personnel working on the study, (4) submit data collection forms for review by the Chairman, IRB, and (5) provide Research Administration Service with accurate status reports for this protocol prior to leaving her position as Chief, Limb Preservation Service, Madigan Army Medical Center.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205013	<b>Status:</b> Ongoing
<b>Title:</b> A Double-blind, Randomized, Placebo-controlled Phase 2b Study to Establish the Effective Dose Range and to Evaluate the Safety of Chrysalin in Adult Subjects with a Fractured Distal Radius		
<b>Principal Investigator:</b> COL Sean D. Ghidella, MC		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Christopher C. Hills, MC; CPT Sarah D. Beshlian, MC		
<b>Start - Completion:</b> 3/3/2005 - Jan 2008	<b>Funding:</b> Orthologic via HMJ	<b>Periodic Review:</b> 10/24/2006

**Study Objective:** Primary Objective: To determine the time to removal of all rigid immobilization used to stabilize fracture after single injection of Chrysalin (1ug, 3ug, 10ug, 30ug) or placebo. Secondary Objective: To compare clinical assessment of bone healing, inflammation, edema, motion, and pain at fracture site, as well as to compare radiographic evaluation with global assessment of bone healing. Safety data will be collected on incidence and severity of emergent adverse events and laboratory assessments.

**Technical Approach:** This trial is a double-blind, randomized, placebo-controlled study to establish the effective dose range of a single percutaneous injection of Chrysalin (1ug, 3ug, 10ug or 30ug) in subjects being treated with surgical reduction of a distal radial fracture. At MAMC, the study will be conducted by the Orthopedic Service. 15-20 MAMC subjects may be enrolled for a total of 500 subjects to be enrolled in the study overall. Subjects will be consented and screened in the orthopedic service in collaboration with the research nurse. Subjects will then be scheduled for surgical reduction on a weekday, within a schedule that allows time for pre-study assessments to be done. Study assessments will include physical examination and history, baseline radiographs, pain questionnaire, CBC, serum chemistry, EKG, and serum HCG as appropriate, prior to study treatment. Chrysalin or placebo will be administered under fluoroscopic guidance in the OR as a single percutaneous injection, after surgical reduction of the fracture. Objective response to treatment will be measured with serial radiographs, grip strength and range of motion. Ongoing efficacy and safety evaluations will include, subject-rated pain scales and laboratory tests. Subjects will be followed by the Orthopedic Service for 52 weeks, including a referral to hand therapy for a minimum of 4 weekly sessions.

The primary analysis will be performed including all subjects who received their study injection and have had at least 8 weeks of follow-up. A secondary analysis will use a modified intent-to-treat sample including all subjects who have received study drug, regardless of follow-up. Safety analyses will include all enrolled subjects. Subjects who become pregnant will be followed to determine the outcome of the pregnancy.

**Progress:** This protocol closed to enrollment with four subjects enrolled; three completed all study visits, and one remains in follow-up until February 2007. Three adverse events were reported but assessed as unrelated to study participation.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206009	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized Study of Volar Fixed-Angle Plate Fixation Versus Closed Management for Fractures of the Distal Radius		
<b>Principal Investigator:</b> COL Sean D. Ghidella, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC John G. DeVine, MC; COL Edward D. Arrington, MC; Elizabeth E. Miklos-Essenber, PT; CPT Aaron H. Hoblet, MC; CPT Joshua P. Herzog, MC		
<b>Start - Completion:</b> 4/19/2006 - Apr 2007	<b>Funding:</b> via Geneva	<b>Periodic Review:</b> 9/29/2006

**Study Objective:** To determine the effectiveness of a volar fixed angle plate in distal radius fractures.

**Technical Approach:** The study will enroll 20 patients in each arm for a total of 40 patients. Subjects will have to meet the following inclusion criteria: 18-99 year old, Distal Radius Fracture, Active Lifestyle, Able to tolerate an operation., Articular Step-off <2mm, Articular Diastasis of <2mm, < 20 deg of dorsal angulation and dorsal comminution of >1/3 of the AP diameter of the radial shaft. Subjects will be excluded for volar oblique fracture (Volar Bartons), die punch fractures, associated DRUJ injury, and associated trauma (polytrauma). Subjects will be evaluated via the following outcomes: at time zero, 6 Weeks, 3 Months (M), 6 M, 12 M, 18 M and 24 M: Grip/Pinch strength, ROM, SF-36, Patient-rated wrist evaluation questionnaire (PRWE), DASH, Missed work days, Time (days) till Radiographic Union, and Complications.

**Progress:** Funding for this protocol has become available. Enrollment remains pending receipt of a CRADA/SOW from The Geneva Foundation and the CRADA/SOW approval process through MAMC DCI, CJA and CIRO.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205079	<b>Status:</b> Ongoing
<b>Title:</b> Microsurgery Training Utilizing The Rat (rattus norvegicus) as a Teaching Model		
<b>Principal Investigator:</b> COL Sean D. Ghidella, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC John G. DeVine, MC; LTC Paul L. Benfanti, MC; MAJ Karen C. Baker, MC; COL Edward D. Arrington, MC		
<b>Start - Completion:</b> 7/13/2005 - May 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7/30/2006

**Study Objective:** The establishment of a microsurgical laboratory utilizing appropriate inanimate materials and anesthetized rats for the teaching and practice of microsurgical techniques will significantly enhance the skills of MAMC surgical staff and residents. It will also correct a deficiency in the Orthopedic Surgery Residency Program (lack of formal micro surgical training) identified by the Residency Review Committee for Orthopedics. Availability of such a laboratory for skill maintenance and enhancement is the standard at teaching institutions that perform microsurgery.

**Technical Approach:** BASIC MICROSURGICAL TECHNIQUES COURSE: This course will consist of five days of progressive microsurgical techniques utilizing didactic or videotape instruction, inanimate "dry labs" for basic instrumentation/orientation training, and practice of prescribed microsurgical procedures utilizing live rats under general anesthesia. The general course flow and animal utilization will be as follows: Day 1: 1) Orientation, course objectives; 2) Basic principles/applications of microsurgery -care and use of surgical microscopes and instruments; 3) Microsurgical instrument lab; 4) Microsuture handling/knot tying/tissue handling; 5) suturing/tissue/handling/"arteriotomy" repair lab with inanimate training materials. Day 2: 1) Rat care and use in microsurgery training; 2) Principles/techniques for end-to-end (ETE) arterial anastomosis; 3) ETE anastomosis-basic technique lab using inanimate training materials; 4) ETE arterial anastomosis lab using live, anesthetized rat. Day 3: 1) Principles/techniques for ETE venous anastomosis. 2) ETE venous anastomosis lab with live, anesthetized rat; 3) Principles/techniques for end-to-side (ETS) arterial anastomosis; 4) ETS arterial anastomosis lab with live, anesthetized rats. Day 4: 1) Principles/techniques for interpositional venous graft; 2) Interpositional venous graft lab with live, anesthetized rats; 3) Principles/techniques for neurorrhaphy; 4) neurorrhaphy lab with live, anesthetized rats. Day 5: 1) Specialty-specific instruction/laboratory with live, anesthetized rats; 2) Vasovasostomy. 3) Fallopian tube anastomosis; 4) Micro-tendon repair; 5) Free vascular tissue transfer; 6) Course Summary/Review/Critique.

**UROGENITAL (OB/GYN, UROLOGY) MICROSURGERY TRAINING:** This course will consist of two (2) consecutive, eight (8) hour days of training in the instrumentation, principles and performance of common urogenital microsurgery techniques and procedures. Course content will generally, but not necessarily follow the detailed synopsis below. Day 1: Introduction to microsurgery (video, slides, written materials, discussion). Day 2: Principles of urogenital surgical site assessment and repair (video, slides, written materials, discussion).

**ADVANCED MICROSURGERY TECHNIQUES (AMT) COURSE:** Advanced microsurgery courses will consist of five (5) consecutive, eight (8) hour training days. Participants in advanced microsurgery training course will plan their proposed advanced procedures with the course instructor(s) prior to course commencement. Course instructors will confer with the DCI Veterinarian regarding proposed advanced procedures and animal species preferences at least 30 days prior to course commencement, in order to ensure adequate consideration for animal



availability, care and postoperative well being. Advanced procedures may consist of techniques such as limb/digit replantation, free vascularized soft tissue or bone grafts, advance neurologic or urogenital reconstructions, anatomical augmentation, organ transplantation, etc. NOTE: Because of the variety of subspecialty-specific procedures to be considered for AMT training, it is not feasible to list or describe specific procedures in this protocol. AMT course schedules and proposed procedures will require MAMC IACUC approval PRIOR to course commencement. Training coordinators for AMT courses will provide reasonable description of the proposed procedures, in writing and will discuss potential procedure-specific post-operative complications for consideration during IACUC review of proposed AMT course schedules.

Day 1: Introduction to microsurgery (video, slides, written materials, discussion) Instrumentation and instrument handling, suture and supplies, suture manipulation and knot tying (video, slides, written materials, discussion) Proper use of the surgical microscope and surgical loupes, suture manipulation and knot tying (laboratory exercise; inanimate training materials) Procedures for end-to-end (ETE), end-to-side (ETS), and side-to-side (STS) anastomosis of tubular organs, and longitudinal defect repair (video, slides, written materials, discussion- Practice ETE, ETS, and STS tubular anastomoses, and longitudinal defect repair (laboratory exercise; inanimate training materials or rat cadaver). Day 2: Principles of urogenital surgical site assessment and repair (video, slides, written materials, discussion) Preparation and suturing techniques for fallopian tube or vas deferens repair/reconstruction (video, slides, written materials, discussion. Practice fallopian tube or vas deferens repair/reconstruction techniques using rat uterus and femoral artery/vein, with surgical loupes and microscope (laboratory exercise; anesthetized rat) Elective instrumentation/procedures laboratory session (e.g. continuation of tubal/vas deferens reconstruction/repair techniques; ureteral injury repair techniques; basic microvascular, microneural, microlymphatic repair techniques; urogenital applications of the non-penetrating Vascular Closure System- VCS, US Surgical Inc. etc) (laboratory exercise; inanimate tissue or anesthetized rat)

#### ADVANCED MICROSURGERY TECHNIQUES (AMT) COURSE:

Advanced microsurgery courses will consist of five (5) consecutive, eight (8) hour training days. Participants in advanced microsurgery training course will plan their proposed advanced procedures with the course instructor(s) prior to course commencement. Course instructors will confer with the CIF veterinarian regarding proposed advanced procedures and animal species preferences at least 30 days prior to course commencement, in order to ensure adequate consideration for animal availability, care, and postoperative well being. /advanced procedures may consist of techniques such as limb/digit replantation, free vascularized soft tissue or bone grafts, advance neurologic or urogenital reconstructions, anatomical augmentation, organ transplantation, etc. Note: Because of the variety of sub-specialty specific procedures to be considered for AMT training, it is not feasible to list or describe specific procedures in this protocol. AMT course schedules and proposed procedures will require 60 MDG IACUC approval PRIOR to course commencement. Training coordinators for AMT courses will provide reasonable description of the proposed procedures, in writing, and will discuss potential procedure-specific postoperative complications for consideration during IACUC review of proposed AMT course schedules. Day 1: Review of microsurgery principles and techniques (video, slides, written materials, discussion. Presentations/discussion of first proposed advanced procedures, including postoperative management/monitoring issues, etc. (video, slides, written materials, discussion. Practice first advance procedures-terminal /non-survival; instructor evaluation of participant technical proficiencies (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat terminal/non-survival. Day 2: Perform advance procedures described on Day 1, morning and practiced Day 1, afternoon; recovery of anesthetized animal (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat. Postoperative assessment of morning surgery animal/operative site; presentations/discussion of second proposed advanced procedures, including postoperative management/monitoring issues, etc. (video, slides, written materials, discussion. Day 3: Assessment of Day 2 animal/operative site;

perform advanced procedures described Day 2 afternoon on new animal; recovery of anesthetized animal (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat. Presentations/discussions of third proposed advance procedure, including postoperative management/monitoring issues, etc.; Postoperative assessment of morning surgery animal/operative site, and Day 2 animal /operative site (video, slides, written materials, discussion); Day 4: Assessment of Day 2 & 3 animals/operative sites; perform advanced procedures; Presentations/discussion of fourth proposed advanced procedures, including postoperative management/monitoring issues, etc.; postoperative assessment of Day 3 animal/operative site (video, slides, written materials, discussion); Day 5: Assessment of Day 3 animal/operative site; perform advanced procedures animal- terminal/non-survival procedure (laboratory exercise; anesthetized rat, rabbit, pig, sheep/goat, terminal/non-survival).

**Progress:** One training lab was held, using two rats for microsurgery training. Four urology residents were trained during the lab.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201112	<b>Status:</b> Completed
<b>Title:</b> Post-operative Shoulder Pain: A Prospective Randomized Trial Comparing the Pain Infusion Pump to the Pre-induction Interscalene Block		
<b>Principal Investigator:</b> CPT Joshua P. Herzog, MC		
<b>Department:</b> Surgery/Orthopedic Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Edward D. Arrington, MC; MAJ Daniel W. White, MC		
<b>Start - Completion:</b> 9/14/2001 - Feb 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** Determine the efficacy of the pain control infusion pump (PCIP) in controlling post-operative pain in patients undergoing shoulder surgery.

**Technical Approach:** This study will enroll 50 consecutive patients scheduled for elective shoulder surgery to address subacromial impingement syndrome with or without a rotator cuff tear; or, acromio-clavicular degenerative disease. Randomization of consented patients to Group A (pain control infusion pump) or Group B (pre-induction interscalene block) will be determined during the preoperative evaluation. Group A patients will undergo surgery and then have the catheter placed in the subacromial space and attached to the "On'Q Pain Management System" with a standardized dose of 0.5% Marcaine. Group B patients will undergo a standardized pre-induction interscalene block utilizing the current standard technique by the anesthesia provider with 0.5% Marcaine. All patients will receive standardized anesthesia and post-operative standard of care, including a PCA for IV narcotic use overnight. The amount of narcotic use, pain medications, nausea medications and difficulties will be recorded. A questionnaire will be completed the day after surgery and will consist of a 10-centimeter visual analog scale for pain, nausea, and pain control satisfaction as well as narcotic and non-narcotic analgesic use tabulation.

Patients will follow-up at 72 to 96 hours for operative site evaluation. The total use of all narcotic and non-narcotic pain meds will be recorded from the time of discharge to this appointment. Group A patients will have the pain control infusion pump catheter removed, the number of narcotic and non-narcotic pain meds used totaled and the same questionnaire used previously completed. Patients will keep a running total of all narcotic and non-narcotic pain meds used from the time of this appointment until the follow-up 7 to 8 days after surgery. At that time the same questionnaire will be administered. Any complications will be continuously followed and data collected until the condition has been resolved, stabilizes, or the study is concluded.

A power analysis will be completed after 10 patients have completed the three questionnaires. Data analyzed: comparison of visual analog scores for pain, nausea, and overall pain control satisfaction. Direct comparison: amount of narcotic and non-narcotic pain medications used. Based on the statistical analysis and the power analysis, the study population size will be determined based on the number of patients that will be required to achieve statistically significant results. The study will then be continued until the appropriate number of patients has been enrolled.

**Progress:** This protocol was reported as completed during FY06, with fifty subjects enrolled. An interim analysis was conducted with 44 data sets; 23 pain control infusion pump and 21 interscalene block. Although results showed increased nausea for the pain controlled infusion pump on post-operative day 3, both pain control mechanism seem to have equal efficacy. It was determined though a new power analysis that 1,200 subjects would be needed to determine statistical significance. This protocol was presented at the Western Orthopaedic Annual Meeting.

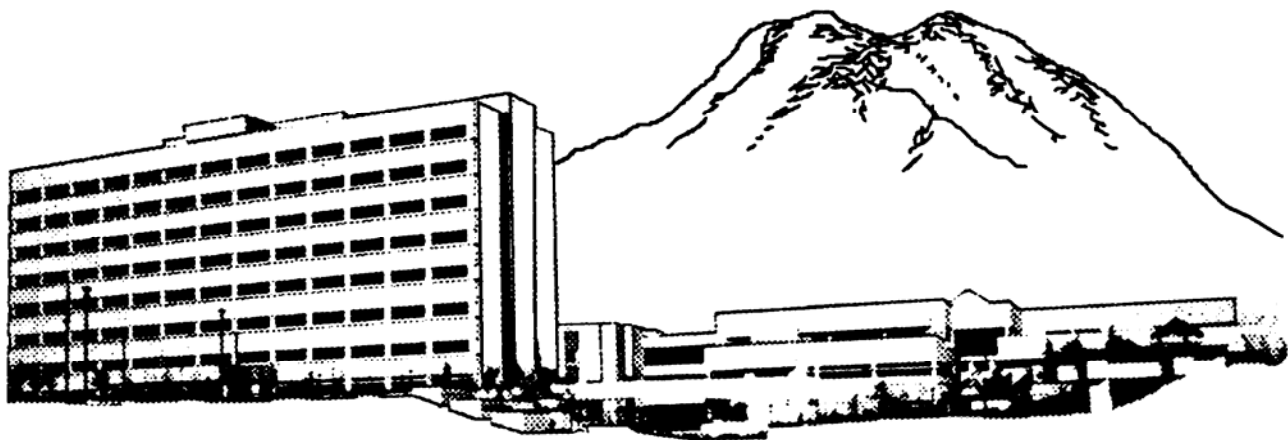
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202091	<b>Status:</b> Terminated
<b>Title:</b> A Prospective, Randomized, Stratified, Parallel Group, Comparison Study of the Healing Rate of Chronic Neuropathic Ulcers Treated with Hyalofill versus Regranex		
<b>Principal Investigator:</b> Monica H. Schweinberger, DPM		
<b>Department:</b> Surgery/Orthopedic Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; Gary P. Degen, DPM; Vickie R. Driver, DPM		
<b>Start - Completion:</b> 10/8/2002 - Jun 2003	<b>Funding:</b> Convatec via The Geneva Foundation	<b>Periodic Review:</b> 6/28/2005

**Study Objective:** Compare the treatment time required for complete wound repair of two wound healing products currently available for diabetic wound care (Hyalofill VS Regranex).

**Technical Approach:** This is a prospective, randomized, stratified, comparative, parallel group, one center clinic trial, comparing the time to wound closure of indolent ulcers healed by Hyalofill protocol of wound care to protocol of Regranex gel. MAMC will enroll 55 total patients. Patient will be stratified according to ulcer location to randomization and will be assigned to either Regranex or Hyalofill protocol. All subjects will participate in the 20 week study or to complete 100% re-epithelization, whichever occurs first. Time to wound closure will be measured in weekly increments.

**Progress:** This protocol was terminated by Dr. Schweinberger in July 2006. The original PI, Dr. Driver, left MAMC employment in November 2005, and the staff of Limb Preservation Service had no interest in pursuing this topic. There are no analyses or study results to present. A total of 20 patients enrolled in this study at MAMC; 14 received study treatment, 3 were screen failures and 3 were removed by the previous PI.



## Detail Summary Sheets

Otolaryngology Service, Department of  
Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204009	<b>Status:</b> Completed
<b>Title:</b> Evaluation of Dizziness / Vertigo by MRI/MRA: A Clinical Outcomes Study		
<b>Principal Investigator:</b> MAJ Brian J. Baumgartner, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 10/31/2003 - Mar 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/15/2004

**Study Objective:** To ascertain the clinical usefulness of obtaining magnetic resonance imaging or magnetic resonance angiography studies of the posterior fossa for the patient with isolated dizziness or vertigo.

**Technical Approach:** Retrospective chart review of all patients over the age of 18 who have had a MRI and/or MRA of the posterior fossa with the words dizziness and/or vertigo in the reason for request field will be performed. The MRI/MRA results will be reviewed. Their charts will then be identified and reviewed to ascertain the indications for the study. The records will be reviewed for the diagnosis and for management decisions based on the MRI/MRA to ascertain the clinical usefulness of this study for the above indications.

**Progress:** Research Administration Service requested that the HUC approve a change of status for this protocol from ongoing to completed, as a final report was submitted last year and the PI has been non-responsive to requests for information via Outlook. HUC approved closure of this protocol in November 2005.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205052	<b>Status:</b> Ongoing
<b>Title:</b> MET™ Fully Implantable Ossicular Stimulator Clinical Trial Protocol		
<b>Principal Investigator:</b> MAJ James V. Crawford, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Carlos R. Esquivel, MC; LTC Dale A. Ostler, MS		
<b>Start - Completion:</b> 5/31/2005 - May 2008	<b>Funding:</b> DCI via Otologics, LLC	<b>Periodic Review:</b> 8/14/2006

**Study Objective:** To determine the safety and effectiveness of a Fully Implantable hearing device.

**Technical Approach:** The Fully-Implantable MET Ossicular Stimulator is an implanted prosthetic device, which bypasses the external auditory canal and mechanically stimulates the ossicles directly to take advantage of the patient's residual hearing. This system is intended to provide amplification with adequate gain, output and superior sound quality to that achieved with conventional, acoustic hearing aids. The target population includes patients who also want the convenience, and features of a fully implantable device which will provide them with amplification in situations where acoustic hearing aids were prohibited such as showering, swimming, sleeping, and various recreational activities.

A Phase I and II multi-site, clinical trial will be conducted with up to 90 patients at 15 investigational sites. The safety endpoints of air and bone conduction are assessed at 3, 6 and 12 month post implantation test intervals to demonstrate that residual hearing is not clinically, significantly affected by the implantation of the fully implantable device. The efficacy endpoints at each test interval are to demonstrate that the fully implantable hearing system is equal to or better than an appropriately fit air conduction hearing aid. The particular areas of comparison are for audibility of soft sounds, speech understanding in quiet and in noise, and perceived benefit by the patient as determined by a questionnaire. The approach to design and analysis has features of single-subject studies, reflecting repeated-measures, within-subjects design, wherein each subject acts as his/her own control.

**Progress:** This protocol was not initiated at MAMC during FY06; however, the company producing the implants received FDA approval and enrollment can proceed.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204042	<b>Status:</b> Terminated
<b>Title:</b> Rapid Employment of Acetylcysteine Treatment for Otologic Recovery (REACTOR), A Prospective, Multicenter, Randomized, Double-blind, Parallel, Placebo-controlled Study Assessing the Efficacy of the Nutritional Supplement N-Acetylcysteine Treatment of Acute Acoustic Trauma		
<b>Principal Investigator:</b> MAJ James V. Crawford, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Douglas M. Sorensen, MC; Allyson A. Peterson, RN; Paul B. Asetre, RN; LTC John J. Simmer, MC; CPT Dan F. Ohama, MS; Vincent D. Eusterman, MD; MAJ Marjorie A. M. Grantham, MS; LTC Dale A. Ostler, MS; LTC Carlos R. Esquivel, MC		
<b>Start - Completion:</b> 4/20/2004 - Jun 2005	<b>Funding:</b> Dept. of the Navy (BUMED) via MIPR	<b>Periodic Review:</b> 4/10/2006

**Study Objective:** To determine if the administration of oral N-Acetylcysteine within the four hours following acute acoustic trauma, sustained by soldiers in the course of military training, can reduce permanent hearing loss, reduce tinnitus severity, and increase the speed of recovery from temporary hearing loss.

**Technical Approach:** This is a prospective, multicenter, randomized, double-blind, parallel, placebo-controlled study assessing the efficacy of the nutritional supplement N-Acetylcysteine treatment of acute acoustic trauma in approximately 190 male and female soldiers across four sites. Subjects will be recruited during routine weapons training following self-reported hearing loss symptoms. Each potential subject will undergo screening audiogram and based on the results be returned to training or referred for additional evaluation. Eligible subjects will be asked to complete a tinnitus questionnaire, a demographics and noise exposure history questionnaire, and then be randomized to either N-Acetylcysteine (NAC) or placebo. Each subject will continue on study medication for seven days and return for audiometric testing and follow-up questionnaires on Days 2 through 4 and again on Day 7, Day 30, and Day 90.

Outcome measures include: (1) mean absolute hearing threshold at each frequency in each ear at each follow-up interval, (2) mean change from baseline (threshold shift) at each frequency in the same ear, at each follow-up interval, (3) mean change from baseline (threshold shift) in the average frequencies of 2,3,4K HZ (most sensitive to noise trauma) in each ear at each follow-up interval and at 30 days, (4) mean improvement (change from worst level) at each frequency in the same ear at 30 days, (5) rate of recovery from worst hearing level at each frequency and at the 2,3,4 kHz average over the study period, (6) mean tinnitus loudness score (0-10) at each follow-up interval compared between treatment groups, (7) frequency of report of subjective hearing difficulty (yes/no) compared between treatment groups, and (8) following independent variables compared between treatment groups: (a) noise exposure characteristics, (b) age, (c) race and ethnicity distribution, (d) baseline hearing thresholds, (e) hearing thresholds at the time of initial evaluation, (f) reported use of medications, and g) smoking history compared between treatment groups.

**Progress:** This protocol has been terminated due to difficulty enrolling subjects at all sites of this multi-center study. Over 40 subjects were screened to date, but none met enrollment criteria.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206058	<b>Status:</b> Completed
<b>Title:</b> Effect of Smoking on Rate of Post-tonsillectomy Hemorrhage		
<b>Principal Investigator:</b> CPT Sean M. Demars, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ James V. Crawford, MC; CPT Wayne J. Harsha, MC		
<b>Start - Completion:</b> 1/31/2006 - Feb 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the effect of smoking on the incidence of post-tonsillectomy hemorrhage in adults at MAMC over the last five years

**Technical Approach:** A search of ORMA will be performed to identify all patients treated by the otolaryngology service from June 2000 to September 2005. This subset of patients will then be further divided to isolate those older than 18 who underwent a tonsillectomy as either the primary or secondary procedure for any diagnosis. Special note will be made of any patients with the preoperative diagnosis of post-tonsillectomy bleed or control of post-tonsillectomy hemorrhage. The billing department will also be contacted to identify all patients with the CPT codes of 42826 and 42821 corresponding to tonsillectomy and adenotonsillectomy greater than 12 years of age respectively. Patients with CPT codes for varying severities of oropharyngeal hemorrhage control (42960-62) will also be collected. These two subsets of patient will be combined and any repetitions will be removed. Also to be removed are all patients younger than 18 and patients undergoing tonsillectomy for oropharyngeal or head and neck cancer. The records of the remaining patients will be evaluated to determine if the patients admitted to currently smoking in either the initial preoperative exam in the otolaryngology clinic, or in the preoperative examination performed by anesthesia. The records would further be searched to determine which patients sought medical attention within 15 days of their surgery and why. The rate of post-tonsillectomy hemorrhage in smokers vs. non-smokers would then be compared using the chi-squared test to determine statistical significance.

**Progress:** This protocol was reported as completed during FY06, with 1,014 chart reviews conducted. A poster was presented at AAO-HNS meeting in September, submission for publication is pending.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206044	<b>Status:</b> Completed
<b>Title:</b> Review of Postoperative Complications after BAHA Implantation at Madigan AMC and Virginia Mason MC		
<b>Principal Investigator:</b> CPT Sean M. Demars, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Carlos R. Esquivel, MC; Douglas D. Backous, MD		
<b>Start - Completion:</b> 1/9/2006 - Jan 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To determine the rate and type of postoperative complications from bone anchored hearing aid placement (BAHA) at MAMC and VMMC.

**Technical Approach:** This study is a retrospective chart review including all patients that have had BAHA placement at either Madigan AMC or Virginia Mason MC in the last five years; focusing on the number and type of complications associated with BAHA placement. Rates of various complications will be reported along with any need for additional procedures or course of antibiotics, any failure of osseointegration or loss of implant, and any skin reactions around the implant.

**Progress:** This protocol was reported completed during FY06, with 81 patients included in the chart review. A poster presentation is pending at the Western Sectional meeting of the Triological Society in February 2007. Submission for publication is also pending.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205050	<b>Status:</b> Ongoing
<b>Title:</b> Celecoxib Versus Oxycodone in Uvulopalatopharyngoplasty Surgery: A Comparison of Post-Operative Risks and Benefits		
<b>Principal Investigator:</b> CPT Matthew R. Grafenberg, MC		
<b>Department:</b> Surgery/Otolaryngology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Vincent D. Eusterman, MD; CPT Roy F. Thomas, MC		
<b>Start - Completion:</b> 9/28/2005 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/26/2006

**Study Objective:** To determine if the drug valdecoxib (Bextra) is associated with less pain, nausea, bleeding and total cost as compared to oxycodone when used in the immediate pre- and post-operative period with uvulopalatopharyngoplasty (UPPP) surgery.

**Technical Approach:** All patients 18 years or older who are diagnosed as having heroic snoring or obstructive sleep apnea syndrome (OSAS) and deemed appropriate surgical candidates based on history and physical exam are eligible for inclusion in this study. There will be approximately 75 patients randomly assigned to three different study groups, (2 experimental and one control). These groups include (1) patients receiving a single pre-operative dose of Bextra and post-operative placebo, (2) patients receiving a pre-operative dose of placebo and post-operative Bextra (20 mg x 5d) and (3) patients receiving both pre-operative and post-operative placebo. Patients will be contacted 14 days after surgery with telephone calls to ensure completion of pain/nausea logs. A post-operative visit at 4 weeks will be scheduled.

The primary outcome variables will be duration/total amount of narcotic usage (oxycodone) and pain scores. Secondary outcome variables will include post-operative nausea and vomiting, bleeding and cost analysis. The number of days and total amount of narcotic usage will be calculated for each of the three study groups. Pain and nausea/vomiting will be measured by visual analog scales (VAS). Bleeding rates will be calculated based on those patients requiring intervention to stop bleeding either in the emergency room (ER) or the operating room (OR) by an ENT physician. Cost will be calculated based on price of medications used for each study group, additional unscheduled clinic visits and any ER/OR interventions performed.

**Progress:** This protocol remains open to patient entry at MAMC; however enrollment has not yet been initiated due to deployments of study staff.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205120	<b>Status:</b> Ongoing
<b>Title:</b> Complications and Audiologic/Tympanometric Findings in Children with Cleft Lip/Palate and Cleft Palate		
<b>Principal Investigator:</b> CPT Matthew R. Grafenberg, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Carlos R. Esquivel, MC		
<b>Start - Completion:</b> 8/18/2005 - Sep 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/10/2006

**Study Objective:** To determine if the surgical procedure of myringotomy with tympanostomy tube placement is associated with an increased risk of complications as compared with no surgical intervention in the cleft lip/palate and cleft palate population.

**Technical Approach:** This is a retrospective chart review of 88 patients, 18 years of age and younger, diagnosed with cleft lip/palate or cleft palate treated at MAMC over a 15-year period. Children with craniofacial anomalies without cleft/palate or cleft palate and those children with isolated cleft lip or cleft lip and alveolus will be excluded from the study. Patients will be divided into multiple groups based on type of cleft and whether surgical intervention with myringotomy and ventilation tube placement was performed. Comparisons will be made between groups with respect to complication types and rates, audiologic findings, tympanometric findings and functionality of tube as described above in the dependent variables section. The primary outcome variables will be complication rates, audiologic and tympanometric results. Other outcome variables will include the effect of cleft type on the need for at least one surgical procedure, effect of cleft type on the total number of surgical procedures, effect of cleft type on average age of 1st surgical procedure and average duration of functional tube based on both type of cleft and tube.

**Data Analysis:** Complication rates will be analyzed and compared on several different fronts. Patients will be divided into those that underwent surgical intervention and those that did not to determine if an association exists between surgical intervention and complication rate. In the group of patients where complications were noted to occur, the average number of ventilation tubes per patient will be calculated and compared to the group of patients that had ventilation tubes placed but no complications to determine if there is an association between increased number of procedures and complication rates. In addition, complication rates will be calculated for each type of tube and a comparison made between groups. Types of complications will also be calculated for each variety of tube and a comparison made between groups. Audiologic results will be reported as pure tone averages (PTA) as previously described. Overall PTA will be calculated for both patients undergoing surgical intervention and those that did not to determine if an association exists between hearing status and tube placement. In addition, both groups of patients will be further broken down according to cleft type to determine if this factor has any effect on hearing status. Those patients undergoing myringotomy with ventilation tube placement will be broken down into pre- and post-operative PTA values to determine if surgical intervention had an immediate short-term effect on hearing. In addition, long-term PTA at approximately 1 and 5 years after initial myringotomy with ventilation tube placement will be calculated for the surgical group (as previously described) and comparisons made to both the original pre-operative and non-surgical group PTA values to determine if surgical intervention has a long-term effect on hearing. Tympanometric results will be classified as normal or abnormal based on criteria previously described. Patients will once again be divided into two groups based whether they underwent surgical intervention. Comparisons between the two groups will be made to determine if an association exists between abnormal tympanograms and surgical intervention. In addition, each group will be further broken down by cleft type to determine if this variable had any effect on

tympanogram results. Other outcome measures to be analyzed include the effect of cleft type on the need for at least one surgical procedure, effect of cleft type on the total number of surgical procedures, effect of cleft type on average age of the 1st surgical procedure and the average duration of functional ventilation tube based both on type of cleft and tube.

**Progress:** This retrospective review protocol has completed data collection from 88 subject charts. Statistical analysis is being conducted. No further chart reviews will be required.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206125	<b>Status:</b> Ongoing
<b>Title:</b> Base of Tongue Reduction for Persistent Obstructive Sleep Apnea Using the Coblator II System: A Pilot Study		
<b>Principal Investigator:</b> CPT James M. Poss, MC		
<b>Department:</b> Surgery/Otolaryngology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Samuel A. Spear, MC, USAF; MAJ Mark A. Criswell, MC		
<b>Start - Completion:</b> 11/17/2006 - Jun 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate the efficacy of coblator reduction of base of tongue in patients who have persistent obstructive sleep apnea (OSA) after prior palate surgery.

**Technical Approach:** Reduction of Base of Tongue with Coblator II plasma wand with integrated cable (8000 J delivered over 2 minutes). Three separate lesions will be made at each of three sites (midline and paramedian bilaterally). Three procedures will take place separated by a time period of at least 1 month.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 26 September 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206020	<b>Status:</b> Ongoing
<b>Title:</b> Clinical Survey of Community Physicians: Post-Tympanostomy Tube Placement and Swimming Precautions/Treatment Otitis Media with Effusion		
<b>Principal Investigator:</b> CPT James M. Poss, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ James V. Crawford, MC		
<b>Start - Completion:</b> 11/30/2005 - Dec 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objective: to determine the differences regarding Post-tympanostomy Swimming Precautions and treatment of Otitis Media with Effusion between Otolaryngologists, Pediatricians, and Family Practice physicians.

**Technical Approach:** Anonymous information will be placed into a database whereby simple statistical analyses can be performed (averages, means, Chi-squared) to look for statistical significance.

**Progress:** Questionnaires were forwarded to 1,116 otolaryngologists, pediatricians and family practitioners in the Pacific Northwest. Over 200 practitioners responded to the questionnaires. The data was presented in poster format at AAO-HNS annual meeting in September 2006. The protocol remains ongoing to complete final paper for submission to a peer reviewed journal.

**Conclusions:** Recommendations for swimming precautions are not universal between the medical specialties that routinely see patients with tympanostomy tubes. Most primary care physicians and many otolaryngologists continue to prescribe water precautions to patients with tubes in place, despite published articles that have shown no reduction in the incidence of otorrhea from barrier devices or avoidance of swimming.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203016	<b>Status:</b> Expired
<b>Title:</b> Pediatric Bronchoesophagology Laboratory Using Swine (Sus scrofa)		
<b>Principal Investigator:</b> LTC Douglas M. Sorensen, MC		
<b>Department:</b> Surgery/Otolaryngology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Andrew Inglis, M.D.; MAJ Andrew B. Silva, MC		
<b>Start - Completion:</b> 10/9/2002 - Oct 2005	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/14/2005

**Study Objective:** To familiarize the junior otolaryngology residents at MAMC and the UW and the Pediatric Surgery fellows at CHMC, with the endoscopic instrumentation and techniques required to evaluate and treat the tracheobronchial tree and esophagus in children. This would include familiarization with esophageal and tracheal foreign body removal, rigid and flexible endoscopic techniques and endobronchial laser use. Familiarity with these techniques would allow an increased margin of safety for children undergoing these procedures and better prepare the endoscopist to assist and then perform these procedures when necessary. Increased endoscopic training experiences will increase operative efficiency and minimize the potential operative risks involved in these procedures.

**Technical Approach:** This is a 4-hour afternoon laboratory session. The LARS, under the supervision of an attending veterinarian, will administer the anesthesia. During this time, 3 pigs will be anesthetized under general anesthesia using IM Rompun/ketamine (2.2mg/kg 20mg/kg). LARS will then obtain intravenous access. Once an adequate plan of anesthesia has been reached, the course participants will perform rigid and flexible bronchoscopy with extraction of a foreign body and esophagoscopy under the supervision of an attending endoscopist. In order to maximize the number of procedures that can be performed within the shortest amount of anesthetic exposure, three live animal stations will be used. The first and second station will be used to teach rigid endoscopy and foreign body removal. The third station will be used to teach flexible endoscopy and foreign body removal. There will also be two additional teaching stations. One will involve instrument set up and use, while the other will involve a teaching station for removal of a safety pin.

Approximately 20 endoscopic procedures will be performed on each animal. Foreign bodies will be used that reproduce those encountered in clinical practices (peanuts, beans, Lego). The foreign bodies will be endoscopically placed and extracted from the bronchus and trachea, under direct vision of the participants and instructors. At the end of the laboratory session, the pigs will be euthanized while they are still under general anesthesia in accordance with the IAW LARS SOP for euthanasia.

All course participants will perform bronchoscopies and foreign body removal on models prior to operating on the swine. The course participants will also participate in a half-day didactic component prior to the laboratory session and will be required to undergo a post course quiz. Completion of the training will be determined by the participant's ability to successfully, and atraumatically perform a bronchoscopy and esophagoscopy with airway foreign body removal.

**Progress:** Protocol is expired Oct 2005, no labs done in FY 06. New protocol submitted and approved to continue this training.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206030	<b>Status:</b> Ongoing
<b>Title:</b> Pediatric Bronchoesophagology Laboratory using Swine ( <i>Sus scrofa</i> )		
<b>Principal Investigator:</b> LTC Douglas M. Sorensen, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> None.		
<b>Start - Completion:</b> 3/8/2006 - Dec 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Skills used to remove foreign bodies in the airway or the esophagus are difficult to develop, taking years of training. To enhance and perfect these skills one must practice. This is best done in a laboratory setting with animal models. A laboratory allows the student to become familiar with the equipment used in pediatric endoscopy and reduplicates the real life setting closely. This ensures a level of technical proficiency that would enable the student to safely and successfully perform endoscopy and endoscopic procedures on children.

**Technical Approach:** Training Design: Animals, usually swine, are fully anesthetized by the certified veterinarian and his assistants. Under the supervision and instruction of board certified staff Otolaryngologists, bronchoesophagology procedures are performed on the animals by the residents. Procedures include direct laryngoscopy, rigid bronchoscopy, rigid esophagoscopy, and endoscopic removal of foreign bodies. The animals are sacrificed after all residents have completed training in the procedures.

**Anticipated Outcome:** Increased proficiency in broncho-esophagology procedures. The junior resident is better prepared to actually perform these procedures in pediatric patients. The more experienced residents are able to sharpen their proficiency on pediatric broncho-esophagology.

**Clinical Application:** The more experienced residents are able to sharpen their proficiency in pediatric broncho-esophagology. The junior resident is better prepared to actually perform these procedures in pediatric patients.

**Progress:** This training protocol was updated and submitted for IACUC approval during FY06. No training labs were held during FY06. A training lab is planned for FY07.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204070	<b>Status:</b> Ongoing
<b>Title:</b> Perioperative Immunonutrition in Head and Neck Cancer		
<b>Principal Investigator:</b> LTC Douglas M. Sorensen, MC		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Mary S. McCarthy, RN, PhD; MAJ Brian J. Baumgartner, MC; LTC Susan G. Smith, AN; CPT Katherine A. Simonson, AN; Vincent D. Eusterman, MD; CPT Sean M. Demars, MC; Evelyn B. Elshaw, RD, MS		
<b>Start - Completion:</b> 7/20/2004 - Oct 2005	<b>Funding:</b> Triservice Nursing Research Program via The Geneva Foundation	<b>Periodic Review:</b> 4/25/2006

**Study Objective:** (1) To determine the feasibility of providing perioperative nutritional support to a convenience sample of undernourished adults undergoing surgery for head and neck cancer. (2) To compare the difference in the nutritional parameters, albumin and prealbumin, between adult patients receiving IEN support or standard nutrition support administered before and after surgery for head and neck cancer. (3) To compare the difference in immune response measured by cutaneous delayed-type hypersensitivity testing, lymphocyte counts, and lymphocyte subset counts between adult patients randomized to receive either IEN support or standard nutrition support administered before and after surgery for head and neck cancer. (4) To compare the difference in surgical wound healing measured by visual inspection between adult patients randomized to receive either IEN support or standard nutrition support administered before and after surgery for head and neck cancer.

**Technical Approach:** On the day that consent is obtained demographic information will be recorded for age, gender, height, weight, diagnosis, risk factors, tumor category, and prior radiation therapy. Also, subjects will complete their section of the subjective global assessment (SGA) tool. Body fat analysis, indirect calorimetry (IC), and dietitian (RD) consultation will be performed. The speech language pathologist (SLP) will also examine the patient briefly to determine if any oral intake is safe. Subjects meeting criteria for inclusion into the study will be randomized to the experimental or control feeding group by the Research Associate.

Once the consent form is signed the surgery date will be noted and the first home visit will be set up with the patient for 8 days prior to surgery. Subjects will have baseline laboratory tests (albumin, prealbumin, T & B lymphocytes, and lymphocyte subsets) drawn on Day-8 or prior to initiating feedings (such as during the preoperative workup). A delayed cutaneous hypersensitivity test will also be placed by the immunization clinic prior to initiating the protocol. During the first home visit, any teaching given by the nursing staff regarding the feeding tube in the hospital will be reinforced and the RA will demonstrate proper use and care of the feeding device. The schedule for feedings (both oral and by feeding device) will also be reviewed with study groups. The RA will distribute the formula to all subjects when making the first home visit. Subjects will receive enough formula to administer >1 liter each day for 7 days. Containers will be labeled with the day and suggested time for infusion as well as numbered for accountability. The RA will also provide each subject with a diary. This diary will be used to record reasons for not following the feeding protocol, gastrointestinal symptoms, feelings/emotions, or questions to ask the investigators.

Each day for the next 6 days of preoperative feeding the RA will phone the subject and ask about adherence to the feeding protocol, difficulties with the feeding tube, or general concerns. Subjects will be reminded to save all formula containers and to bring them to the hospital the day of surgery. Postoperative follow-up visits occur with the ENT surgeon on a weekly basis. These visits will provide the perfect forum for the multidisciplinary research team to meet with the patient and

assist with any care issues that have developed since discharge. On POD 15, 22, and 29, a wound healing assessment will be performed by the physician and nurse jointly. On POD 29 the subject has completed the interventional study period and the PI/RA will record data regarding hospital outcomes, wound healing outcomes, and infectious complications.

**Progress:** This protocol has closed to enrollment, with fifteen patients enrolled who completed the study. Data analysis is ongoing. Perioperative nutrition support was found to be feasible and favorably accepted by patients and staff. Subjects did not vary in demographics at baseline. Preliminary analyses suggest a trend of less immune suppression (measured by CD4, CD8, and CD4:8 ratio) in the treatment group (TG) who received immune-modulating nutrition support for seven days pre- and post-operatively compared to the control group who received standard nutrition support. Patients were followed for three-weeks postoperatively to assess wound healing and infectious complications. No adverse events occurred during the study.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206057	<b>Status:</b> Ongoing
<b>Title:</b> Review of Thyroid Cancer Treatment Outcomes at a Major Medical Center from 1996-2000		
<b>Principal Investigator:</b> CPT Samuel A. Spear, MC, USAF		
<b>Department:</b> Surgery/Otolaryngology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Douglas M. Sorensen, MC		
<b>Start - Completion:</b> 1/31/2006 - Jan 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** This will be a retrospective chart review of patients diagnosed with thyroid cancer at Madigan Army Medical Center from 1996 to 2000 to determine the effect of clinical and treatment factors on local tumor control, control of distant metastasis, recurrence, survival, and complications in all patients diagnosed and treated with differentiated thyroid carcinoma.

**Technical Approach:** All the records of patients diagnosed and treated for thyroid carcinoma at Madigan Army Medical Center from 1996-2000 will be identified through the MAMC pathology database, MAMC tumor-registry records and MAMC outpatient medical records and reviewed. Individual patient data will be collected with regards to age at diagnosis, gender, ethnicity, date of last known follow-up, initial FNA result, the presence of positive lymph nodes or metastases, the staging at diagnosis, the original tumor size, the histological type, the surgical treatment, any adjuvant therapy, any complications, recurrence date and location, treatment of the recurrence, mortality, cause of death, & disease free period. Data will be entered into an Excel spreadsheet for further evaluation and analysis.

**Progress:** Medical records of patients newly diagnosed and treated for thyroid cancer at Madigan Army Medical Center (MAMC) from 1996-2000 were identified and examined. Eighty-two (82) patients were identified as being treated for new onset thyroid carcinoma at this medical facility from 1996-2000, of which all were eligible for review. Initial review and statistical analysis is complete. Results were presented as a poster presentation at the Madigan Army Medical Center Research Day in May 2006, and also presented at the 2006 AAO-HNSF Annual Meeting and at the OTO EXPO in Toronto, California, September 2006. The protocol remains ongoing to conduct the final statistical analysis, along with a paper submission to a medical journal.

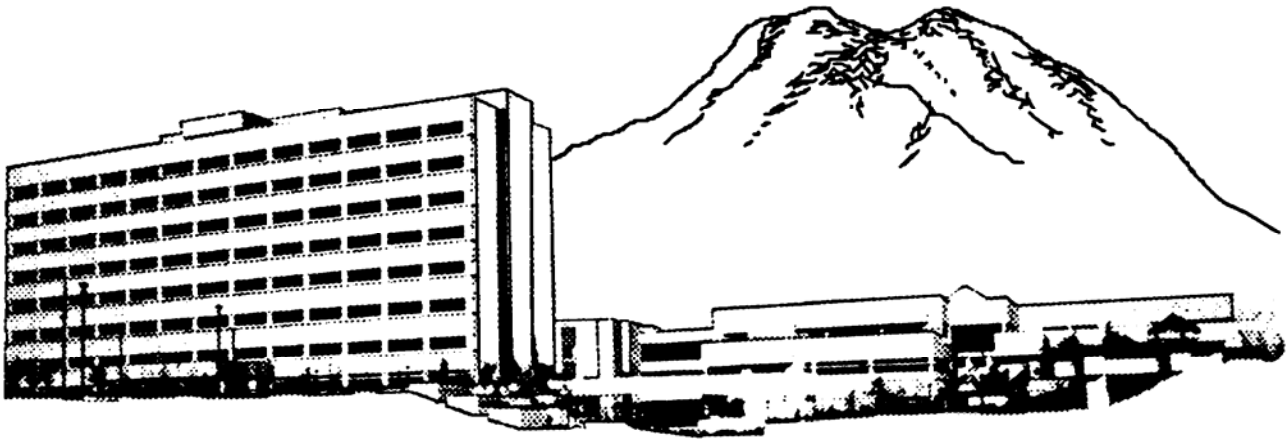
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205009	<b>Status:</b> Ongoing
<b>Title:</b> Inferior Turbinate Reduction Comparing Turbinate Microdebrider, Coblation and Bipolar Cautery		
<b>Principal Investigator:</b> CPT Roy F. Thomas, MC		
<b>Department:</b> Surgery/Otolaryngology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Jamie Hanson, MC; CPT Matthew R. Grafenberg, MC		
<b>Start - Completion:</b> 3/11/2005 - Apr 2006	<b>Funding:</b> Arthrocare via Geneva Foundation	<b>Periodic Review:</b> 10/26/2006

**Study Objective:** To determine the efficacy of inferior turbinoplasty using three accepted methods: turbinate microdebrider, coblation or submucous diathermy.

**Technical Approach:** This is a prospective, single blinded, randomized trial to compare use of a turbinate microdebrider, coblation and bipolar cautery device to determine if use of the microdebrider or coblator results in increased nasal volumes, decreased symptom scores and decreased nasal crusting when compared with turbinate bipolar. 90 patients, 30 per arm, will be recruited from patients referred to ENT with complaints of nasal obstruction. After informed consent is obtained, baseline evaluations will include history and physical exam, rhinoscopy, acoustic rhinometry and symptom scores. Patients will be randomized to receive turbinate reduction via turbinate microdebrider, coblator or bipolar. Follow up examinations will take place at 1 week, 2 weeks, 1 month and three months. Nasal crusting will be graded at 1 week, 2 weeks and 1 month. Symptom scores, rhinoscopy and acoustic rhinoscopy will be performed at 3 and 6 months. Comparisons will be made between baseline and postoperative data and between treatment groups. Results in change of volume from acoustic rhinometry will be evaluated with ANOVA to compare change in volume between the three arms of the study. Change in symptom scores between the three arms will be compared with the Kruskal Wallis test.

**Progress:** This protocol remains ongoing; however, enrollment was delayed by approval of coblator machine for use in OR. Has since been cleared by CJA and all needed equipment is ready, staff are trained, and enrollment can commence. Study is still pertinent and numbers should accumulate rapidly.



## **Detail Summary Sheets**

Urology Service, Department of Surgery

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205129	<b>Status:</b> Terminated
<b>Title:</b> A Multi-Center, Open-Label Evaluation of the Safety of Silodosin in the Treatment of the Signs and Symptoms of Benign Prostatic Hyperplasia, Protocol #SI040011		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Andrew C. Peterson, MC		
<b>Start - Completion:</b> 1/9/2006 - Jul 2006	<b>Funding:</b> Watson Laboratories, Inc. via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective is to evaluate the safety of silodosin 8 mg given once daily for 40 weeks as measured by adverse events, vital signs, electrocardiograms, clinical laboratory tests, and physical examination. The secondary objective is to evaluate the sustained efficacy of silodosin 8 mg given once daily for 40 weeks for the relief of the signs and symptoms of benign prostatic hyperplasia as measured by changes in score of the International Prostate Symptoms Score-1 and maximum urine flow rate.

**Technical Approach:** This is a multi-center, open-label 40 week investigation of up to 1200 men with signs and symptoms of BPH. This study will serve as an open-label extension for BPH patients who have previously completed a 12-week double-blind investigation of silodosin (SI04009 or SI04010), with Visit 1 of this study occurring on the same day as the last visit of the double-blind study. Note that some data from the previous double-blind study (demographics, medical and medication history from Visit 1, and physical examination, ECG, clinical labs, vital signs, IPSS-1, Qmax, concomitant medication from Visit 8) will be carried over for this study. Silodosin 8 mg once daily with food at breakfast will be administered each day. Seven visits will occur at weeks 0, 2, 8, 16, 24, 32, and 40 or discharge. Informed consent will be obtained at Visit 1. A physical exam will be performed at visit 7 or discharge. ECGs will be obtained at Visits 3 and 7 or discharge. Clinical laboratory tests will be performed at Visits 3, 4, and 7 or discharge. Vital signs will be performed at Visits 3, 4, and 7 or discharge. The IPSS-1 questionnaire will be administered at Visit 3 and 7 or discharge. Measurements of Qmax will occur at Visits 3 and 7 or discharge. Adverse events will be monitored at every visit after drug dispensing. Concomitant medications will be monitored at every visit. Investigational product compliance will be reviewed at all visits after drug dispensing.

**Progress:** The study sponsor terminated this protocol as of 27 June 2006, and will not be completing a study close out visit since MAMC was never activated as a study site and no patients were enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205092	<b>Status:</b> Ongoing
<b>Title:</b> A Multi-center, Randomized Clinical Investigation of Trelstar™ Versus Continued Therapy in Patients Receiving Lupron or Zoladex for Advanced Prostate Cancer		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Andrew C. Peterson, MC		
<b>Start - Completion:</b> 10/27/2005 - Jul 2007	<b>Funding:</b> Pharmatech, Inc. via Henry M. Jackson Foundation	<b>Periodic Review:</b> 7/20/2006

**Study Objective:** Primary Objective: to compare the inhibitory effect of Trelstar™ versus Lupron or Zoladex on serum testosterone level in patients with advanced prostate cancer. Secondary Objectives: (1) To compare the degree of testosterone suppression by Trelstar™ versus Lupron or Zoladex, (2) To compare the safety and tolerability of Trelstar™ therapy versus Lupron or Zoladex therapy, and

**Technical Approach:** Male patients from the Department of Urology who are currently receiving hormonal therapy for advanced prostate cancer will be offered this research protocol. Subjects will be randomized in a 1:1 ratio to either continuation with current therapy (Lupron or Zoladex) or to study drug (Trelstar), given on a monthly or every three month basis depending on their current treatment schedule. Response will be measured with laboratory tests for testosterone and PSA, and adverse event recording at Baseline and Day 85. Adverse events will be compared with respect to number and severity of events. 95% confidence intervals will be computed for the differences between the Trelstar group and the Continuing therapy group.

**Progress:** This protocol remains open to enrollment with no subjects screened or consented during FY06.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205072	<b>Status:</b> Completed
<b>Title:</b> A Multi-Center, Randomized, Double-Blind, Placebo Controlled, Parallel Evaluation of the Efficacy and Safety of Silodosin in the Treatment of the Signs and Symptoms of Benign Prostatic Hyperplasia, Protocol # SI04009		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Andrew C. Peterson, MC		
<b>Start - Completion:</b> 7/8/2005 - Apr 2006	<b>Funding:</b> Watson Laboratories, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 4/25/2006

**Study Objective:** Primary objective: The primary objective of the trial is to test the hypothesis that the effectiveness of silodosin 8 mg given once daily for 12 weeks is superior to placebo for the relief of symptoms of benign prostatic hyperplasia as measured by a baseline to endpoint change in the total score of the International Prostate Symptoms Score-1(IPSS-1). Secondary objectives. (2) To test the hypothesis that the effectiveness of silodosin is superior to placebo based on a baseline to endpoint change in the maximum urine flow rate (Qmax). (2) To compare the safety of silodosin to placebo using an evaluation of adverse events, vital signs, ECGs, clinical laboratory tests, and physical exams.

**Technical Approach:** This is a multicenter, double-blind, placebo controlled, parallel, 12 week treatment trial in a sufficient number of men with signs and symptoms of BPH, such that 600 are randomized. Screening will occur within 4 weeks of Visit 1. A 4-week single-blind placebo run-in period will be followed by 12 weeks of therapy with silodosin 8 mg, or placebo, once daily with food at breakfast. Nine visits will occur at screening and weeks -4, -2, 0, 0.5, 1, 2, 4, and 12 or discharge. Informed consent will be obtained at screening. A physical exam will be performed at Visits 1 and 8 or discharge. ECGs will be obtained at Visits 1, 7, and 8, or discharge. Clinical laboratory tests will be performed at screening and Visits 1, 7, and 8 or discharge. Vital signs will be performed at Visits 1, 3, 7, and 8 or discharge, with an orthostasis test being included on Visits 1, and pre- and post-dose on Visit 3. The IPSS-1 questionnaire will be administered at each visit to the clinic after screening, including an additional test being completed over the telephone 3 days after Visit 1 while the patient is available to conduct a candid phone conversation. Measurements of Qmax will occur at Visits 1, 2, 3, (pre- and 2-6 hours post-dose), 5, 6, 7, and 8 or discharge. A plasma sample for the pharmacokinetic analysis of silodosin and major metabolites will be obtained at Visits 3 (2-6 hours after first dose) and 7 (2 to 6 hours post-dosing). Adverse events will be monitored at every visit after drug dispensing (including placebo). Concomitant medications will be monitored at every visit. Investigational product compliance will be reviewed at all visits after drug dispensing.

**Progress:** A study site close out visit was conducted in June 2006. Seven MAMC subjects were screened; two were randomized and completed the study. Four subjects did not meet randomization criteria and were withdrawn and one subject failed screening. No internal adverse events were reported.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203035	<b>Status:</b> Ongoing
<b>Title:</b> A Multi-Institutional Pilot Study to Evaluate Molecular Markers in Urine and Serum in the Early Detection of Prostate Cancer		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Keith J. O'Reilly, MC; MAJ Raymond S. Lance, MC; CPT Jack R. Walter, MC		
<b>Start - Completion:</b> 2/28/2003 - Nov 2003	<b>Funding:</b> NCI	<b>Periodic Review:</b> 1/18/2006

**Study Objective:** The primary objective of this study is to examine whether the presence of tumor-specific gene promoter hypermethylation (e.g., GSTP1, Annexin II, CD44 and Caveolin 1) in serum and/or urine sediments can predict prostate cancer among patients referred to diagnostic biopsy. The secondary objective of this study is to explore whether the presence of tumor-specific gene methylation (e.g., GSTP1, Annexin II, CD44 and Caveolin 1) in core-needle biopsy specimens can predict subsequent disease status in patients who biopsy negative and develop cancer on subsequent biopsy within two years.

**Technical Approach:** 50 men who are between the ages of 40 and 75 years old and require prostate core needle biopsy will be enrolled in this pilot study here at MAMC. At the biopsy visit prior to the procedure the patient will be asked to provide a serum specimen. A 15-30 second prostate massage will be conducted and patients will be asked to provide a 30-50 ml urine specimen within 30 minutes of the massage. Each patient will undergo their scheduled core needle biopsy of the prostate. The number of biopsy cores taken will range from 8-12 which is Standard of Care at MAMC and will be left up to the discretion of the doctor performing the study. The concordance between gene methylation in the serum and urine, and diagnostic biopsy will be determined for all patients. Also methylation status of the tumor specimen will be determined for all cases who receive curative radical prostatectomy. Follow-up with patients will be determined by biopsy results. Length of study follow-up will be five years.

**Progress:** This protocol closed to enrollment with 100 patients enrolled, none during FY06. Follow up clinical data will be collected from the study participants for the next five years. Methylation assay of three genes in question has been completed on the biopsy cores of all 100 patients. The analysis of the urine samples is ongoing.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201113	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III, Extension Study to Evaluate the Safety of 10 mg Atrasentan in Men with Hormone-Refractory Prostate Cancer (M00-258)		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; ; MAJ Michael J. Sebesta, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 9/4/2001 - Jul 2002	<b>Funding:</b> Abbott Labs via The Geneva Foundation	<b>Periodic Review:</b> 5/23/2006
<b>Study Objective:</b> To evaluate the safety of 10 mg Atrasentan for the treatment of prostate cancer. In addition, the pharmacokinetic parameters of Atrasentan will be defined in a sub-population of subjects.		
<b>Technical Approach:</b> This is a phase III, open label study evaluating the safety of 10 mg Atrasentan in men with hormone refractory prostate cancer. All men enrolled in this protocol must have successfully met all of the eligibility criteria for this trial and have completed one of the following Phase III trials:		
M00-211: A Phase III, Randomized, Double-Blind, Placebo controlled Study Evaluating the Safety and Efficacy on 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer		
M00-244: A Phase III, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic Hormone Refractory Prostate Cancer		
Eligible men will receive a single, oral dose (soft gelatin capsule) of 10 mg Atrasentan before leaving the clinic (Day 1). They will then continue taking the same dose of study drug once a day at approximately the same time each day. The study participants will be asked to return to the clinic on study days 14, 28, at Week 12, and then every 12 weeks thereafter. Upon study completion subjects will be asked to come into the clinic for a final assessment, and will return again for a safety evaluation 30 days after the last dose of study drug. Blood will be drawn at every visit. Urine samples will be obtained at visit Day 1, Day 28, every 12 weeks and at final visit.		
<b>Progress:</b> This is an extension protocol to study #201121. Six patients enrolled overall at MAMC, one during FY06. Four patients completed the study, one patient was discontinued and one patient remains active. The protocol is now closed to patient entry.		

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201107	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Metastatic, Hormone-Refractory Prostate Cancer (M00-211)		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; MAJ Keith J. O'Reilly, MC; MAJ Henry E. Ruiz, MC; CPT Jack R. Walter, MC; MAJ Leah P. McMann, MC; MAJ Sunil K. Ahuja, MC; MAJ Thomas L. Poulton, MC; COL Raymond A. Costabile, MC; MAJ Raymond S. Lance, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 9/4/2001 - Jul 2002	<b>Funding:</b> Abbott Labs via The Geneva Foundation	<b>Periodic Review:</b> 6/8/2006

**Study Objective:** 1) To evaluate the safety and efficacy as measured by time-to-disease progression. 2) To evaluate the effect of 10 mg Atrasentan on: PSA progression, Biochemical bone markers, Bone scan index, Survival and to evaluate the effect of the study drug on quality of life and performance status and to perform population pharmacokinetic analysis.

**Technical Approach:** This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg Atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. The patient will then enter the screening phase, which will last 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. The patient will be randomized in a 1:1 ratio to receive either Atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Participants will be assigned a 4-digit study number and will be given study drug prior to leaving the clinic. Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. Participants will visit the clinic on Day 14, Weeks 4, 8, & 12, and every 6 weeks thereafter. At each visit the participants will be assessed for safety, clinical evidence of disease progression and will be dispensed study medication. They will be evaluated for disease progression by radiographic imaging every 12 weeks and as needed if participant experiences symptoms suspected to be related to disease progression. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends (as defined by when 650 subjects have experienced confirmed events of disease progression). The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above.

**Progress:** This study closed to patient entry in February 2003, with eight subjects screened, six randomized, four who completed the study, one screen failure and one who withdrew consent. Four internal serious adverse events were reported during the active study period. There are no

patients continuing to be followed under this protocol. The study remains ongoing at MAMC pending a formal site close out visit with the study sponsor.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 201121	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of 10 mg Atrasentan in Men with Non-Metastatic, Hormone-Refractory Prostate Cancer (M00-244)		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 10/11/2001 - Sep 2002	<b>Funding:</b> Abbott Labs via The Geneva Foundation	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** Primary: To evaluate the safety and efficacy as measured by time-to-disease progression.

Secondary: (1) To evaluate the effect of 10 mg Atrasentan on: PSA progression, Biochemical bone markers, Bone scan index, (2) Survival, (3) To evaluate the effect of the study drug on quality of life and performance status and (4) To perform population pharmacokinetic analysis.

**Technical Approach:** This is a phase III, multicenter, multinational trial evaluating the safety and efficacy of 10 mg Atrasentan in men with metastatic, hormone refractory prostate cancer. The men participating in this study have been diagnosed with hormone-refractory prostate cancer that has been treated with surgical and/or chemical castration but is now escaping androgen suppression as demonstrated by rising PSA. There must also be evidence of distant metastasis. The patient will then enter the screening phase, which will last less than or equal to 35 days and will include EKG, laboratory tests, medical history and physical examination. CT scan (or MRI) & bone scan will be performed. A copy of all scans will be sent to a Central Imaging Center within 2 weeks of collection. After the patient has met eligibility criteria, the patient will be randomized in a 1:1 ratio to receive either Atrasentan or a placebo (Day 1) via an Interactive Voice Response System (IVRS). Study medication will then be taken once a day at approximately the same time each day except for at Weeks 4 & 12 when a trough blood specimen will need to be drawn. At those two visits the patient will take the study medication after all laboratory specimens have been drawn. The subject will be considered to have completed the study if he has experienced an event of disease progression that has been confirmed by an independent reviewer, or is active in the trial when the double-blind treatment period ends. The subject will then be eligible to enter the open label extension study. If he declines to participate in the extension study, he will be asked to return for safety evaluation 30 days after their final visit. Subjects will be assessed for post-treatment survival at 3-month intervals after the last study visit. Someone who did not complete the study (premature withdrawal) will not be eligible to enter the extension study, but will be asked to continue coming in for visits as outlined above.

**Progress:** This protocol closed to patient entry 31 March 2003, with nine patients enrolled at MAMC. Seven patients completed the clinical trial and two patients withdrew consent. Two patients have been rolled over into the (M00-258) extension trial within the last 12 months. There are currently no patients on active study medication, but continue to receive survival status follow-up calls.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204005	<b>Status:</b> Ongoing
<b>Title:</b> A Phase III, Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Ability of Risedronate to Prevent Skeletal Related Events in Patients with Metastatic Prostate Cancer Commencing Hormonal Therapy, Protocol #GU02-41		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; ; MAJ Michael J. Sebesta, MC; MAJ Jasmine T. Daniels, MC; LTC David E. McCune, MC; MAJ Angela G. Mysliwiec, MC; CPT Jennifer M. Pugliese, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 1/29/2004 - Oct 2004	<b>Funding:</b> Hoosier Oncology Group via The Geneva Foundation	<b>Periodic Review:</b> 10/24/2006

**Study Objective:** (1) To evaluate the ability of a daily oral dose of 30 mg risedronate as compared with placebo to prevent skeletal complications in patients undergoing androgen deprivation for metastatic prostate cancer by measuring the time to a skeletal-related event (SRE). (2) To evaluate a daily oral dose of 30 mg risedronate compared to placebo in patients undergoing androgen deprivation for metastatic prostate cancer with respect to the following: (a) The rate and the duration of the serological response by measuring the changes in prostate-specific antigen (PSA) levels, (b) The effect on tumor response by measuring the response rate after 6 months of therapy by radiographic means. (c) Time to development of hormone refractory disease. (d) The changes in biochemical markers of bone turnover. (e) Overall survival. (f) The safety and the tolerability as determined by frequency and severity of treatment-emergent adverse events.

**Technical Approach:** This is a randomized, placebo-controlled, double-blind, multicenter, stratified, 2-arm study. Up to 360 evaluable subjects will be enrolled at approximately 50 study sites. After stratification based on age, performance status, and severity of metastatic disease, subjects will be randomized at a 1:1 ratio to the following treatment arms: (a) Daily risedronate combined with androgen deprivation, and (b) Daily oral placebo combined with androgen deprivation. The study population will consist of prostate cancer subjects with metastatic bone disease for whom androgen-deprivation therapy is planned. Subjects will be registered to the study within 3 days before beginning risedronate or placebo and may begin androgen-deprivation therapy 7 days before beginning risedronate or placebo. The subject will receive treatment of one 30-mg tablet/placebo oral per day every morning. Subject is to take risedronate/placebo with 6-8 oz of water 30 minutes before the first food or drink of the day and should not lie down for 30 minutes after taking. Subjects will receive concomitant treatment with calcium carbonate at a dose of at least 500 mg orally per day every evening. Subjects will receive concomitant treatment with vitamin D at a dose of at least 400 IU. Subjects will remain in the study for at least 12 weeks, but may continue for 2 years or longer depending on progression of disease. They will be seen in the clinic every 4 weeks for the first 12 weeks and every 12 weeks thereafter.

**Progress:** This protocol is closed to enrollment with four patients enrolled. One patient has been lost to follow-up and one patient remains active on study treatment. The other patients continued to be followed during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204122	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Double Blind, Placebo Controlled, Four Arm (Placebo, Tolterodine ER, Tamsulosin, and Tolterodine ER plus Tamsulosin) Study to Evaluate the Clinical Efficacy and Safety of Tolterodine ER 4 mg in Men who have Frequency and Urgency, with or without Urinary Urge Incontinence, with or without Bladder Outlet Obstruction, Protocol Number A6121120		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Andrew C. Peterson, MC; MAJ Keith J. O'Reilly, MC; CPT Brian J. DeCastro, MC		
<b>Start - Completion:</b> 12/2/2004 - Sep 2005	<b>Funding:</b> Pfizer via The Geneva Foundation	<b>Periodic Review:</b> 9/27/2005

**Study Objective:** Primary objective of the trial is to evaluate the effect of tolterodine ER plus tamsulosin versus placebo on patient perception of overall treatment benefit in men who have frequency and urgency, with or without urinary urge incontinence (UI), with or without bladder outlet obstruction (BOO). Secondary objective is to evaluate the effect of, Tolterodine ER vs. placebo, Tolterodine ER plus tamsulosin vs. tamsulosin, Tolterodine ER plus tamsulosin vs. tolterodine ER, Tamsulosin vs. placebo, and Tamsulosin vs. tolterodine ER on efficacy, safety, patient's perception, health-related quality of life and sexual function in men who have frequency and urgency, with or without UI, with or without BOO.

**Technical Approach:** This is a 12-week randomized, double blind, placebo controlled, four arm (placebo, tolterodine ER, tamsulosin, and tolterodine ER plus tamsulosin) multicenter, United States study to evaluate the effects of tolterodine in men who have frequency and urgency, with or without UI, with or without BOO. 830 adult male subjects, > 50 years of age, will be enrolled in this study. The trial will be conducted at 83 centers with each center enrolling 10 subjects. All subjects will be equally randomized (1:1:1:1) into four groups and will receive placebo, tolterodine ER, tamsulosin, or tolterodine ER plus tamsulosin once a day for 12 weeks. Each group will receive either: Tolterodine ER placebo plus tamsulosin placebo, Tolterodine ER plus tamsulosin placebo, Tolterodine ER placebo plus tamsulosin, or Tolterodine ER plus tamsulosin. Following consent, patients will be screened for inclusion criteria. At Baseline/Visit 2 (Day 0), once study entry has been verified, tests will be performed and study diaries and medication given. Diaries will be reviewed and survey's completed during Visit 3/Week 1 (Day 7 +2). Study medication will be given during Visit 4/Week 6 (Day 42 +2). End of Study Visit 5/Week 12 (Day 84 +2) study staff will review diary, perform tests, and patients will complete surveys. Study staff will complete the Subject Disposition page. There is no scheduled follow up visit after Visit 5/Week 12.

**Progress:** This protocol closed enrollment in January 2006 and a study site close out visit was conducted in July 2006. A total of 23 subjects screened, 16 enrolled, 15 completed and one withdrew consent prior to completion of the study. Seven subjects screen failed for various reasons. No internal serious adverse events were reported.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206100	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-Blind, Multicenter Study of Denosumab Compared with Zoledronic Acid (Zometa®) in the Treatment of Bone Metastases in Men with Hormone-Refractory Prostate Cancer (20050103)		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Jennifer M. Pugliese, MC; ; MAJ Michael J. Sebesta, MC; MAJ Andrew C. Peterson, MC; CPT Brian J. DeCastro, MC; MAJ Mark I. Anderson, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 9/22/2006 - Jun 2011	<b>Funding:</b> Amgen, Inc. via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To determine if denosumab is non-inferior to zoledronic acid (Zometa®) with respect to the first on-study occurrence of a skeletal-related event (SRE) in men with hormone-refractory prostate cancer and bone metastases

**Technical Approach:** This is an international, phase 3, randomized, double-blind, active-controlled study comparing denosumab with zoledronic acid in the treatment of bone metastases in men with hormone-refractory prostate cancer. Approximately 1700 subjects will be randomized in a 1:1 ratio to receive either denosumab, administered at a dose of 120 mg by subcutaneous (SC) injection every 4 weeks (Q4W), or zoledronic acid, administered at a dose of 4 mg (equivalent creatinine clearance-adjusted dose in subjects with baseline creatinine clearance > 60 mL/min) by a single, no less than 15-minute, intravenous (IV) infusion Q4W, in a blinded manner. The randomization will be stratified by previous SRE (yes or no), PSA level (< 10 ng/mL or > 10 ng/mL), and current (defined as within 6 weeks before randomization) chemotherapy for prostate cancer (yes or no). Each subject will receive either an SC injection of denosumab and an IV infusion of zoledronic acid placebo Q4W or an SC injection of denosumab placebo and an IV infusion of zoledronic acid Q4W. Subjects will continue to receive investigational product Q4W until 745 subjects have experienced an SRE (defined as pathological fracture [vertebral or non-vertebral], radiation therapy to bone [including the use of radioisotopes], surgery to bone, or spinal cord compression). Serum denosumab concentration levels will be obtained from a subset of approximately 150 subjects at select centers.

**Progress:** This protocol remains open to patient entry, with no patients enrolled.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206072	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled, Multi-Center Phase 3 Study of Denosumab on Prolonging Bone Metastasis-Free Survival in Men with Hormone-Refractory Prostate Cancer		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; ; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; COL Robert C. Allen, MC; CPT Brian J. DeCastro, MC; MAJ Mark I. Anderson, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 6/8/2006 - Mar 2012	<b>Funding:</b> Amgen, Inc. via Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To compare the treatment effect of denosumab with placebo on prolonging bone metastasis-free survival in men with hormone refractory (androgen independent) prostate cancer who have no bone metastasis at baseline.

**Technical Approach:** This is an international, phase 3, randomized, double blind, placebo controlled study in subjects with hormone refractory (androgen independent) prostate cancer. Approximately 1400 subjects will be randomized in a 1:1 ratio to receive denosumab at a dose of 120 mg, SC, Q4W or placebo, SC, Q4W. The randomization schedule will be stratified based on PSA criteria (PSA level 8.0 ng/mL AND PSA doubling time 10.0 months [yes/no]) and previous or current chemotherapy for prostate cancer (yes/no). Subjects will receive investigational product until the end of treatment. The treatment period will end after approximately 660 subjects have developed bone metastasis or died. Subjects will complete the end of study visit approximately 4 weeks after their last dose of investigational product administration. The study duration (excluding the follow up period) is estimated to be 42 months, which includes an enrollment period of approximately 15 months.

**Progress:** This protocol is open to patient entry, with no patients enrolled during FY06. Active pre-screening for this clinical trial continues.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205006	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Bone Fractures in Men with Prostate Cancer on Androgen Deprivation Therapy (Protocol #G300203)		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 1/20/2005 - Jan 2007	<b>Funding:</b> GTx, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 9/26/2006
<p><b>Study Objective:</b> Primary Objective: To assess the efficacy of toremifene in the prevention of bone fractures in men with prostate cancer on androgen deprivation therapy as measured by semi quantitative assessment of vertebral fractures. Secondary Objectives: (1) To assess the safety profile of toremifene in subjects on androgen deprivation therapy (ADT) for the treatment of prostate cancer. (2) To assess the effect of toremifene on the incidence of clinical fragility fractures. (3) To assess the effect of toremifene on bone mineral density (BMD) of the lumbar spine as assessed by DEXA scan. (4) To assess the effect of toremifene on BMD of the femur as assessed by DEXA scan. (5) To assess the effect of toremifene on the incidence, frequency and severity of hot flashes. (6) To assess the effect of toremifene on the incidence and severity of gynecomastia. (7) To assess the effect of toremifene on quality of life.</p> <p><b>Technical Approach:</b> In a double-blind fashion, qualifying subjects will be equally randomized into one of two treatment groups. Up to 600 subjects will be randomly assigned to receive 60 mg toremifene citrate as two 40 mg tablets and up to 600 subjects will be randomly assigned to receive matching placebo tablets containing no toremifene citrate. All treatments will be administered orally once daily for 24 months. An interim analysis of BMD data will be conducted on the first 200 subjects that complete 12 months of treatment and have baseline and 12 month DEXA assessments. The treatment duration of the study will be 24 months. The beginning of study treatment is defined as the first day of toremifene or placebo administration. Subject clinic visits for this study will include the following: screening, randomization, 3, 6, 9, 12, 15, 18, 21, and 24 months. There will be a screening evaluation including procedures that are necessary to determine subject eligibility prior to receiving study treatment. The site will contact the subject by telephone approximately seven days, but no more than ten days, after the randomization visit. The telephone contact will include assessment of study drug compliance and tolerance. Subsequent phone calls will be made at monthly intervals +/- 1 week to assess drug compliance and track serious adverse events. The subject clinic visits will occur every three months for the duration of the study.</p> <p><b>Progress:</b> This protocol closed to enrollment with two patients enrolled and randomized at MAMC. One subject withdrew consent and one subject was discontinued from the study. Both patients are inactive and no longer receiving treatment. Protocol remains ongoing at MAMC pending final site close out visit by the study sponsor.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204091	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate AMG 162 in the Treatment of Bone Loss in Subjects Undergoing Androgen-Deprivation Therapy for Non-Metastatic Prostate Cancer		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; CPT Brian J. DeCastro, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; CPT Jack R. Walter, MC; Dieter Kirchheim, MD		
<b>Start - Completion:</b> 10/5/2004 - Aug 2006	<b>Funding:</b> Amgen, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** Primary objective is to determine the treatment effect of AMG 162 compared with placebo on lumbar spine bone mineral density (BMD) in men with non-metastatic prostate cancer undergoing Androgen Deprivation Therapy. Secondary objectives are to assess the effect of AMG 162 compared with placebo on the vertebral and non-vertebral fracture incidence, BMD in total hip and femoral neck and to assess the safety and pharmacokinetics of AMG 162 in this population.

**Technical Approach:** This is an international, multi-center, randomized, double-blind, placebo-controlled study in subjects with non-metastatic prostate cancer undergoing androgen deprivation therapy (ADT). Approximately 968 subjects at approximately 150 sites in North America and Europe will be randomly assigned to receive placebo or AMG 162 in a 1:1 allocation ratio. The randomization schedule will be stratified based on age group (= 70, > 70 years of age), and duration of ADT with GnRH agonist, or orchiectomy at the time of study entry (0-6 months vs. > 6 months). Subjects will participate in the study for 24 months. There is a planned interim analysis after subjects complete their one-year (12 month) study evaluation period. Once a subject has been determined eligible to participate in the study written consent must be obtained prior to screening for eligibility. Screening assessments include obtaining a medical history, physical examination, bone scan, radiographs, bone densitometry, and collection of blood for hematology and chemistry. Eligible subjects will return to the site within 28 days of screening for the baseline (day 1) visit, during which baseline-related assessments will be done and subjects randomized. Subjects will return at months 1, 3, 6, 12, 15, 18 and 24 for study related procedures and evaluations. All subjects will take daily calcium (1 gram) and vitamin D (at least 400 IU). All subjects will receive the same volume of study medication (AMG 162 vs. placebo) subcutaneously every 6 months. This study will also explore the effect of AMG 162 on PSA, overall survival, and subject reported outcomes (subject questionnaires).

**Progress:** This protocol closed to enrollment with thirteen patients enrolled, none during FY06. Three patients screen failed and two patients withdrew consent. Eight patients remain on active study medication and continued to be followed during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204025	<b>Status:</b> Completed
<b>Title:</b> An Evaluation of Semen Characteristics after 40 Weeks Daily Dosing with 20 mg Tadalafil		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Raymond A. Costabile, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Mark I. Anderson, MC; MAJ Andrew C. Peterson, MC		
<b>Start - Completion:</b> 2/19/2004 - Nov 2004	<b>Funding:</b> Lilly via The Geneva Foundation	<b>Periodic Review:</b> 11/4/2004

**Study Objective:** (1) To test the null hypothesis that the proportion of subjects who have 50% or more reduction from baseline in sperm concentration in the tadalafil group is less than 0.20 higher than that in the placebo group at 40 weeks. (2) To assess the effect of 20 mg tadalafil administered daily for 40 weeks as compared with placebo on sperm concentration, total sperm number per ejaculate, sperm motility and sperm morphology. (3) To assess the effect of 20 mg tadalafil administered daily for 40 weeks as compared with placebo on serum concentrations of reproductive hormones testosterone (total and free), LH and FSH. 4) To assess the long term safety of tadalafil.

**Technical Approach:** Subjects will include healthy males and males with mild erectile dysfunction. Subjects will receive either 20 mg tadalafil orally once daily or placebo orally once daily. During the 4 week screening phase (Visits 1 & 2) subjects will be assigned a unique ID number for tracking purposes. Ejaculation information will be collected and instructions for 2 semen samples given to subjects. A recall instrument will be given to the subjects to document each sexual encounter during the course of the study: Global Assessment Questions (GAQ, a one time assessment of events over the course of the study) and Psychological and Interpersonal Relationship Scale (PAIRS, a set of scales that assess psychological and relationship aspects of ED and its treatment). During the 40 week double blind treatment phase (between Visits 2-6) eligible subjects will be randomly assigned to either placebo or 20 mg tadalafil at Visit 2 and ejaculation information collected. Visits 3-6 will be scheduled at 12, 22, 32, and 40 weeks from Visit 2, with a visit window of  $\pm$  7 days. Between Visit 3-6, two semen specimens will be collect from each subject within at least 48 hours, but no longer than 5 days sexual abstinence prior to each collection. The two samples will be collected within 1 week on either side of each visit. Early withdrawal information will be collected and data interpreted. Two more samples will be requested prior to discontinuation. Reversibility Phase: Up to 26 weeks without study medication (between Visits 6-8), the reversibility phase may be stopped early as described. Information will be collected during the 13 weeks between visits and semen specimens collect as above. Subjects who demonstrate a clinically significant decrease in sperm concentration may be followed after study completion.

**Progress:** This protocol was reported completed in November 2005. A final site close-out visit by the study sponsor was held 3 November 2005. Five subjects enrolled, four screen failed, and one was randomized and started on the study medication, but became lost to follow-up.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205119	<b>Status:</b> Ongoing
<b>Title:</b> Expression of CXCR4 in Archived Prostate Cancer Specimens and its Association with Patient Demographics, Pathologic Results, and Outcomes		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Brian J. DeCastro, MC; LTC Stephen C. Groo, MC; CPT Joren B. Keylock, MC; CPT Patrick M. McNutt, MS; CPT Jeremy P. Celver, MS; CPT Michael J. Hartenstine, MS; CPT Garth S. Herbert, MC		
<b>Start - Completion:</b> 8/15/2005 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 7/20/2006

**Study Objective:** Our primary objective is to compare CXCR4 expression in prostate cancer cells to benign prostate cells in archived prostate specimens. Our secondary objectives are to examine, to the extent possible, the relationships between CXCR4 expression and patient demographics, pathological characteristics, and disease specific outcomes.

**Technical Approach:** This study is a retrospective review of 100-300 patients who underwent radical retropubic prostatectomy or transurethral resection of the prostate. Pathology specimens obtained from previous prostatectomies and transurethral resections of the prostate will be stained for CXCR4 expression with commercially available antibodies and the intensities will be scored using an ordinal scale as judged by three different investigators. The difference in staining of cancerous tissue and benign prostatic tissue will be compared with a t-test and a p value of 5% will be considered statistically significant. These findings will be coordinated with the patients' clinical course located in outpatient records, CHCS, ICDB, and the CPDR. Differences in CXCR4 expression will be compared to demographic factors such as race and age, and the association with disease specific outcomes.

**Progress:** During FY06, this bench protocol has tried several techniques for immunofluorescence staining for the CXCR4 antigen with mixed and inconsistent results. Investigators are now attempting colormetric staining techniques.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205017	<b>Status:</b> Ongoing
<b>Title:</b> Madigan Army Medical Center Advanced Laparoscopic Training Using the Pig (Sus scrofa)		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Kenneth S. Azarow, MC; MAJ James A. Sebesta, MC; MAJ Alec C. Beekley, MC		
<b>Start - Completion:</b> 11/10/2004 - Nov 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/22/2006

**Study Objective:** Advanced laparoscopic surgical techniques have been developed and are being used with increased frequency. These include techniques upon the stomach especially anti-reflux procedures such as the Nissen fundoplication as well as cholecystectomy and exploring the common bile duct. Laparoscopic techniques for appendectomy, segmental colectomy, total colectomy, colostomy creation, abdominoperineal resection, splenectomy and weight loss surgery have also been developed. The performance of these procedures requires a higher degree of laparoscopic training and skills that must be acquired in the laboratory prior to application in the operating room upon humans. An increased familiarity with these techniques decreases operative time, continues to train staff and residents and minimizes complications for patients while offering state of the art and standard of care surgical services.

**Technical Approach:** To familiarize General Surgery and Urology residents, staff and invited surgeons from our community with techniques in the performance of advanced laparoscopic techniques. This training will include esophagus, stomach, biliary, small & large intestine, spleen, liver retroperitoneal and urological procedures. The training benefit will accrue to General Surgery and Urology residents, Staff and invited surgeons by introducing these techniques or reinforcing earlier acquired skills in a controlled environment. Familiarity with these techniques will allow an increased margin of safety for patients, decreased operative time and minimizing of potential complications.

**Progress:** Protocol is active and training objectives are being met. 14 urology residents were trained in 2 labs and 24 surgery residents were trained in 2 labs.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204121	<b>Status:</b> Terminated
<b>Title:</b> Prevalence of PCR Detectable Human Papillomavirus (HPV) in Sexually Active Males - A Comparison of Specimen Collection Methods and Genitourinary Sites		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Patrick M. McNutt, MS; MAJ Steven D. Mahlen, MS; LTC Andrew R. Wiesen, MC; LTC Carol A. Moores, MC; CPT Hieu V. Hoang, MC		
<b>Start - Completion:</b> 1/20/2005 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 2/3/2006

**Study Objective:** To determine the prevalence of Human Papillomavirus in sexually active males and compare the sensitivities of different methods of specimen collection at different genitourinary sites.

**Technical Approach:** This is a cross-sectional study which plans to enroll 400 subjects. Once consented, subjects will complete a questionnaire and the investigator will review the questionnaire to ensure it is completed, examine the subject, collect the specimens, and complete the data collection sheet. With the exception of the GC/Cz DNA probe, which will be labeled IAW MAMC laboratory policy, the investigator will label all specimen containers with the subject's unique code number and the location from which the specimen was obtained.

After collection the specimens will be refrigerated and transported to the DCI within 8 hours. In the DCI, exfoliated skin specimens will be agitated for 10 minutes and the emery paper and swabs will be removed. The urine specimen will be centrifuged at 10,000g for 10 minutes and the cellular debris will be collected and suspended in a buffered saline solution. 150mcl of the solution from the GC/Cz DNA probe will be pipette into a vial for use in this study and the remainder of the GC/Cz DNA probe sample will be transmitted to the MAMC laboratory and processed in accordance with standard operating procedures. The study specimens will be maintained at -70C until further processing. Subjects with detectable HPV will be sent a formatted letter to inform them of the finding. Results will be reviewed at intervals to ensure the study is adequately powered. A standard statistical package will be used to analyze the results

**Progress:** This protocol was reported terminated in February 2006, after enrolling only 21 of the 400 subjects required. Study staff cited a lack of interest in continuing the study.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206039	<b>Status:</b> Ongoing
<b>Title:</b> SEER Rapid Response Surveillance Study #5, Prostate Cancer Therapy Selection (PCATS) Study		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 1/5/2006 - Oct 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/8/2006

**Study Objective:** The objective of the study is to explore way to improve the treatment experience for men living with prostate cancer and their families.

**Technical Approach:** Madigan Army Medical Center will refer patients to Fred Hutchinson Cancer Research Center for participation in this study. Up to 20 MAMC patients who are not too distressed will be approached if they meet eligibility criteria and asked to complete a "consent to contact" form, which will be faxed via confidential line to FHCRC where all other aspects of the study will be conducted. This is a prospective cohort study of adult men with newly diagnosed localized prostate cancer, recruited from urology clinics in the SEER regions (Puget Sound Region: FHCRC, Los Angeles Region: University of Southern California, and the Greater Bay Area Region: Northern California Cancer Center/Kaiser Permanente). The goal is to enroll a total of 850 subjects; 100 from FHCRC, 150 from USC, and 600 from NCCC/KP. There is no coordinating center, as each study site is funded independently and will be completing the study independently. Final data analyses with de-identified data will be pooled and conducted at NCCC/KP.

**Progress:** This protocol closed to enrollment, with 3 patients enrolled at MAMC. The protocol will remain ongoing at MAMC pending completion of the study at the other sites.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204120	<b>Status:</b> Ongoing
<b>Title:</b> The Effect of Flexible Cystoscopy on the Serum PSA Values		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Brian J. DeCastro, MC; MAJ Mark I. Anderson, MC; MAJ Andrew C. Peterson, MC; CPT Jennifer M. Pugliese, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 2/2/2005 - Nov 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 9/26/2006

**Study Objective:** To determine the affect of flexible cystoscopy on serum PSA values in male patients with prostates.

**Technical Approach:** Free and total PSA values will be obtained in 100 males ages 20 to 79 undergoing flexible cystoscopy to evaluate the effect of flexible cystoscopy on serum PSA values. Because PSA is an important screening test for prostate cancer in men aged 40 through 79, the number of study participants age less than 40 will be limited to 10 participants each for the age groups 20 to 29 and 30 to 39. All men will be volunteers who are already scheduled to undergo flexible cystoscopy. A serum sample for free and total PSA will be drawn up to 1 hour before flexible cystoscopy and will be the baseline value. Serum samples will be drawn again at 1 hour after cystoscopy and the day following cystoscopy. If interval analysis after 30 patients shows no clinically significant difference between the second and third serum samples, the third sample will be eliminated. The PSA values before and after cystoscopy will be compared with a paired t-test or the Wilcoxon signed-rank test. Additional variables that could influence the change in PSA values to include, but not limited to, age, race/ethnicity, prostate size, and reason for cystoscopy will be recorded and analyzed. Multivariate analysis will be applied once univariate analyses are completed.

**Progress:** This protocol closed enrollment after 30 subjects enrolled and an interim analysis showed statistical significance but not clinical significance. A manuscript is in progress.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205040	<b>Status:</b> Ongoing
<b>Title:</b> The Epidemiology of Nephrolithiasis in Soldiers Returning From Operation Iraqi Freedom		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jennifer M. Pugliese, MC; CPT Brian J. DeCastro, MC; MAJ Mark I. Anderson, MC; CPT Jack R. Walter, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Andrew C. Peterson, MC; LTC Maricela Contreras, MC; Charles G. Beleny, MD		
<b>Start - Completion:</b> 2/11/2005 - Nov 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 1/12/2006
<b>Study Objective:</b> To study the epidemiology of nephrolithiasis in soldiers returning from Southwestern Asia.		
<b>Technical Approach:</b> In this four year descriptive, cohort study a database containing demographic, military, medical information will be constructed for soldiers returning from Southwestern Asia who experienced renal colic/nephrolithiasis while deployed. Candidates for the study will be identified by survey during routine post deployment medical screening at the Soldier Readiness Point. Soldiers with a history of urinary calculi or renal colic during their deployment will be referred to the urology clinic evaluation of nephrolithiasis and participation in the database. A CT scan, appropriate serum chemistries, and screening urine test will be performed on all subjects. Investigators hope to better describe the epidemiology of stone disease in soldier deployed in to Southwestern Asia support of Operation Iraqi Freedom and the Global War on Terrorism.		
<b>Progress:</b> This protocol closed to enrollment, with over 6,000 surveys about stone disease collected from military personnel returning from OIF. Only seven service members with stone disease were referred to urology and subsequently consented. Data analysis is ongoing.		

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204079	<b>Status:</b> Ongoing
<b>Title:</b> Uniformed Services University National Prostate Cancer Database for the Center for Prostate Disease Research (CPDR) with Patterns of Care, Outcomes, and Prognostic Analyses, Protocol Number GT90CM		
<b>Principal Investigator:</b> MAJ Karen C. Baker, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 9/22/2004 - Jan 2009	<b>Funding:</b> USUHS via Henry M. Jackson Foundation	<b>Periodic Review:</b> 5/10/2006

**Study Objective:** (1) To collect standardized data on consenting patients treated for prostate disease at specified centers. (2) To maintain an accurate, reliable, secure relational database of patients with prostate disease that meets IRB/HIPPA patient safety, private, and confidentiality guidelines. (3) To coordinate and maintain longitudinal prostate cancer data collection from various sources as a prostate cancer database repository at USUHS. (4) To analyze patterns of care, prognostic factors, quality of life and intermediate and long-term outcomes for prostate cancer and prostate disease entered into this database.

**Technical Approach:** Subjects previously consented in MAMC #98092 will be rolled over into this protocol. Subjects will be asked prospectively to enroll in this database if their doctor recommends that a transrectal ultrasound of the prostate be performed for a medical condition relating to the prostate. Data will be collected and stored in the CPDR database via stand alone data entry. This will include information normally collected on newly diagnosed patients with benign prostatic hypertrophy (BPH) and prostate cancer (CaP) from initial diagnosis to treatment to follow-up care. The development of the CPDR database simply organizes the information into a standard format in order to facilitate the data collection process similar to the hospital tumor registries except that the prostate disease specific information is more comprehensive. Standardized QOL instruments will be employed prior to treatment and periodically during follow-up. The CPDR collaborating statisticians and epidemiologists will be responsible for the quality assessment of the collected data and for the statistical analysis of future research initiatives. The electronic data collected by CPDR will reside in the CPDR National Database and maintained on a secure server at the CPDR Headquarters (part of USUHS) and backed up by the Henry M. Jackson Foundation. The server maintained at CPDR will contain the National Repository for all collaborating sites/locations.

A CPDR research file will be maintained on each subject in locked filing cabinets in the Research Offices of each site. A copy of labs, xrays, bone scans, CT scans, etc., and narrative summaries, operation report(s) related to prostate cancer treatment, radiation therapy summaries, pathology report(s), and death certificates if applicable, will be filed on each patient as well as hard copies of the CPDR forms and the consent form. All sites will use standardized Clinical Research Forms (CRF) which have been designed and can be used as SF600 encounter forms at each patient visit, where permitted. The following data collection forms are used to collect data on all prostate disease patients at participating institutions and are shown and explained in "Forms Manual." (1) Patient Registration, (2) TRUS biopsy, (3) Pre-treatment Staging, (4) Surgery (Radical Prostatectomy), (5) Radical Prostatectomy Pathology, (6) Hormonal Therapy, Chemotherapy and other medications, (7) External Beam Radiation Treatment, (8) Brachytherapy Treatment, (9) Cryotherapy Treatment, (10) Cryotherapy Follow-up, (11) Follow-up, (12) Update of Medical History, (13) CPDR Annual Follow-Up Survey, (14) Necropsy

**Analysis of Data:** The primary purpose of any research database is data analysis to answer

research questions and explore hypotheses. With multiple Site Principal Investigators interested in data analysis, the current system of submitting a CPDR Collaboration consent form will be used. When the study PI, Site PI's or other collaborating researchers want to propose an analysis of multicenter data, a standardized collaboration agreement form will be initiated by the Site PI and his/her CPDR site Research Data Manager. The site personnel will write the proposal in the standardized format and forward it to the Regulatory Affairs Office at CPDR Headquarters. After receiving a CPDR data collaboration request, the Research Opportunity Evaluation Committee at CPDR HQ will discuss the proposal in terms of data availability, statistical support needed, other resources required, military relevance, medical significance and publication probability. If the committee agrees to pursue the proposal and if the request comes from within the CPDR network, the site is asked to prepare the protocol and submit it according to the site's guidelines, while CPDR HQ gets the CPDR collaboration consent from all the sites. Upon receipt of the documentation of approval, CPDR Regulatory Affairs will submit it with a 3204 to USU for approval. Upon receipt of USU approval, the protocol will be forwarded to all contributing sites to prepare and submit to their respective IRB's as required. Approvals will be forwarded to USU REA. If the request comes from outside the CPDR Database network, additional IRB documentation and other appropriate documents specific to the proposal may be requested. These will be submitted to REA with the rest of the submission packet for primary review.

**Progress:** This outcomes database protocol remains open to enrollment, with 69 patients enrolled at MAMC during FY06, for a total of 1,989 patients enrolled since study approval. The CPDR continues to perform data collection.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202065	<b>Status:</b> Ongoing
<b>Title:</b> Oral Ketoconazole For Prevention Of Postoperative Penile Erection, A Prospective, Randomized, Double Blind Trial		
<b>Principal Investigator:</b> CPT Brian J. DeCastro, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Mark I. Anderson, MC; MAJ Andrew C. Peterson, MC; CPT Jack R. Walter, MC; MAJ Leah P. McMann, MC; MAJ Karen C. Baker, MC; COL Raymond A. Costabile, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 5/23/2002 - Dec 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4/25/2006

**Study Objective:** To determine if Ketoconazole adequately prevents penile erections after penile surgery.

**Technical Approach:** This study will be broken into three phases. Phase 1-Patients will be identified in the urology clinic scheduled to undergo penile or urethral surgery. Prior to surgery, they will be offered participation and randomized to receive Ketoconazole or placebo. Forty patients will be randomized in a 1:1 ratio to Ketoconazole or placebo. Phase 2-Forty-eight hours before surgery, the patient will be started on the study drug (Ketoconazole 400 mg or placebo TID for a total treatment period of ten days). They will be administered the study questionnaire to fill out at the end of the treatment period. Phase 3- A follow-up telephone call will be made six weeks postoperatively to assess patient satisfaction with the outcome of surgery.

**Progress:** This protocol completed accrual during FY06, with 43 subjects enrolled. Three extra subjects were required when two subjects withdrew consent without treatment and one subject had surgery cancelled. The protocol remains ongoing for data analysis of 40 usable data sets.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205136	<b>Status:</b> Ongoing
<b>Title:</b> The Incidence of Infection and Stent Colonization in Patients With and Without Strings		
<b>Principal Investigator:</b> CPT Brian J. DeCastro, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Steven D. Mahlen, MS; MAJ Keith J. O'Reilly, MC; MAJ Andrew C. Peterson, MC; MAJ Karen C. Baker, MC; MAJ Mark I. Anderson, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC; CPT Jennifer L. Gurski, MC		
<b>Start - Completion:</b> 1/5/2006 - Aug 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** To determine if the presence of an external string attached to an indwelling ureteral catheter will lead to an increase in the incidence of infection and stent colonization . 2) To determine which patients are at a higher risk of infection and stent colonization.

**Technical Approach:** This study is a prospective randomized study looking at the infection rate of patients with indwelling ureteral stents. Patients will be randomized to two groups. One group will have nylon strings attached to the stent while the second group will have the strings removed at the time of surgery. Urine samples and stent cultures will be used to determine if there is a significant difference in the infection rate of the two groups. Patient demographics will also be analyzed to see if sex, comorbidities, , duration of stent, or indication for stent placement contributed to an increased rate of significant infection or stent colonization. Significance will be determined using the (X2) test with a p value of < 0.05 being significant

**Progress:** No work was conducted under this protocol due to deployment of study staff. Enrollment is expected to begin in March 2007.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205076	<b>Status:</b> Ongoing
<b>Title:</b> Madigan Army Medical Center's Current Clinical Practice and Experience With Osteopenia And Fractures In Men Treated With Androgen Deprivation Therapy		
<b>Principal Investigator:</b> CPT Dayne M. Nelson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Keith J. O'Reilly, MC; MAJ Andrew C. Peterson, MC		
<b>Start - Completion:</b> 5/6/2005 - Mar 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> 4/20/2006

**Study Objective:** To determine the incidence of skeletal morbidity and mortality in patients with prostate cancer receiving androgen deprivation therapy at Madigan, as well as the therapies that are currently being prescribed.

**Technical Approach:** This study is a retrospective review of 96 men with prostate cancer currently receiving Androgen Deprivation Therapy (ADT) in the Urology Clinic, specifically looking at the incidence and risk of skeletal morbidity and mortality. In addition, an army wide survey will be conducted with reference to the risks of ADT and the steps army urologists are taking to prevent and treat skeletal morbidity and mortality. The study will record patient demographics, number of months of ADT, incidence and types of fractures occurring after initiation of ADT, results of bone mineral density (BMD) studies conducted after the initiation of ADT, and the types and frequency of treatment prescribed within our facility. The results of the army-wide survey will also be recorded. Data will be analyzed to determine the incidence of bone loss and bone fracture in our patient population currently receiving ADT. The results of the army-wide survey will also be analyzed to determine the awareness of the skeletal morbidity and mortality associated with ADT and what army urologists are doing to monitor, prevent, and treat these effects.

**Progress:** This protocol remained ongoing during FY06 to complete final the final manuscript.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203053	<b>Status:</b> Completed
<b>Title:</b> A Clinical Trial Evaluating the Safety and Efficacy of ABX-EGF in Patients with Hormone Resistant Prostate Cancer Elevated PSA With or Without Metastasis, Protocol Number ABX-0310		
<b>Principal Investigator:</b> MAJ Keith J. O'Reilly, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Raymond S. Lance, MC; CPT Jack R. Walter, MC; MAJ Leah P. McMann, MC		
<b>Start - Completion:</b> 5/9/2003 - May 2005	<b>Funding:</b> Abgenix/Immunex via The Geneva Foundation	<b>Periodic Review:</b> 3/22/2005
<p><b>Study Objective:</b> Primary objective: To assess the clinical effects determined by the PSA response of multi-dose administration of 2.5 mg/kg ABX-EGF in HRPC patients with rising PSA without metastases. Secondary objectives: (a) To examine the pharmacokinetics (PK), (b) to examine safety profile (including immunogenicity), (c) to assess the overall survival, (d) to evaluate the time to disease progression, and e) to evaluate the time to PSA progression.</p> <p><b>Technical Approach:</b> This study is designed as a multicenter, multiple dose clinical trial to evaluate the safety and effectiveness of administering ABX-EGF in patients with HRPC. Approximately 5 patients will be enrolled here at MAMC. Patients will receive 2.5 mg/kg of ABX-EGF administered IV once a week for 8 weeks per course for a total of 6 treatment courses. The patient will visit the clinic once a week for 8 weeks. If the patient has had no disease progression during the initial treatment period they are eligible for the extended treatment period. If the patient continues with the extended treatment period they will continue to receive 2.5mg/kg of ABX-EGF for up to 10 months (5 additional 8 week courses of treatment). Patients will be continually monitored and reassessed for PSA response every 4 weeks. Patients will attend a safety follow-up visit 4 weeks after their last infusion of ABX-EGF or when the patient is withdrawn from treatment for any reason. All patients will be followed for assessment of survival duration for two year following their first infusion of ABX-EGF. During this time patients will be contacted every three months for survival, status disease status and any cancer medications/therapies information.</p> <p><b>Progress:</b> This protocol closed to enrollment in September 2003, with one patient enrolled at MAMC who completed treatment and the 24 month survival follow-up via telephone. No internal serious adverse events were reported. A final site close out visit was conducted in November 2005.</p>		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205033	<b>Status:</b> Completed
<b>Title:</b> A Phase 2, 8-Week, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study Evaluating the Efficacy, Tolerability and Safety of [S,S]-Reboxetine (PNU-165442G) for Stress Urinary Incontinence in Women, Protocol A6061023		
<b>Principal Investigator:</b> MAJ Keith J. O'Reilly, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; COL Robert C. Allen, MC; MAJ Karen C. Baker, MC; CPT Brian J. DeCastro, MC		
<b>Start - Completion:</b> 4/20/2005 - Jan 2006	<b>Funding:</b> Pfizer via The Geneva Foundation	<b>Periodic Review:</b> 1/18/2006

**Study Objective:** Proof of concept study to assess the efficacy, tolerability and safety of SS-RBX vs. placebo in the treatment of SUI and to evaluate whether an upward dose adjustment affects the tolerability of SS-RBX.

**Technical Approach:** This is a randomized, double-blind, placebo controlled, 4-treatment arms (placebo and 3 active) comprised of 4 phases: (1) Drug free run-in period of 2 weeks, (2) Single blind placebo run-in period of 2 weeks. (3) 8 weeks double blind randomized treatment period and (4) 2 week follow up period. Those subjects entering the 8 week treatment phase will be randomized into the following groups in a 1:1:1:3 ratio: (1) Group 1 SS-RBX 2mg QD, increasing to SS-RBX 4mg QD after 4 weeks, (2) Group 2 SS-RBX 4mg QD for eight weeks, (3) Group 3 SS-RBX 4mg QD, increasing to SS-RBX 6mg QD after 4 weeks and (4) Group 4 Placebo. A follow up visit will occur 2 weeks after the treatment period has been completed. Subjects will not be able to down-titrate their dose. Subjects unable to tolerate study drug will have to be withdrawn from the study. It is expected that approximately 600-800 subjects will be screened in order to randomize 400 subjects. Approximately 40-60 sites will be recruiting into the study. Subjects will undergo stratification at randomization using incontinence episode frequency (Group A <14 episodes/week; Group B > 14 episodes/week. This will be calculated from the self-reported diary data collected just prior to V4 (week 0).

**Progress:** This protocol closed to enrollment 13 February 2006, with no subjects screened or enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206024	<b>Status:</b> Terminated
<b>Title:</b> A Twelve-Week Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Forced Titration, Proof of Concept Study to Assess the Efficacy, Safety and Tolerability as well as the Pharmacokinetic Profile of 60 mg and 120 mg of GW679769 (GW679769) administered once daily vs. Placebo in Women with Overactive Bladder		
<b>Principal Investigator:</b> MAJ Keith J. O'Reilly, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; MAJ Andrew C. Peterson, MC		
<b>Start - Completion:</b> 2/28/2006 - Nov 2006	<b>Funding:</b> GlaxoSmithKline via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary objective is to compare the efficacy of GW679769 administered once daily for 12 weeks (60 mg for 6 weeks, followed by 120 mg for 6 weeks) and placebo in female subjects with overactive bladder (symptoms of urgency with urge incontinence and frequency which may be associated with nocturia).

Secondary objectives are to evaluate the safety and tolerability of GW679769 administered once daily for 12 weeks (60 mg for 6 weeks, followed by 120 mg for 6 weeks) compared to that of placebo in female subjects with overactive bladder (symptoms of urgency with urge incontinence and frequency which may be associated with nocturia); to describe the exposure of both GW679769 and its primary metabolite (GSK525060) after 12 weeks of dosing (60 mg for 6 weeks, followed by 120 mg for 6 weeks) in female subjects with overactive bladder; and to explore the relationship of GW679769 and its primary metabolite (GSK525060) with clinical response/safety after 12 weeks of dosing (60 mg for 6 weeks, followed by 120 mg for 6 weeks) in female subjects with overactive bladder.

**Technical Approach:** This is a phase IIa, multi-center, randomized, double-blind, forced titration, placebo-controlled, parallel group study of GW679769 in female subjects 18 years of age but not older than 65 with OAB with symptoms of urgency with urge incontinence and frequency which may be associated with nocturia but without bladder related pain. The study will consist of a 1 or 2 week treatment-free run-in period followed by a 12 week treatment period. After completion of the treatment period, subjects will return approximately one week later for their follow-up visit.

During the one or two week treatment-free run-in period, subjects will be restricted from taking any medications used to treat OAB and maintain an electronic diary beginning 3 days immediately prior to the randomization visit. If subjects meet the inclusion criteria, they will be randomized into the 12-week, double-blind treatment phase and receive either GW679769 (60 mg and 120 mg) or placebo. After 2 weeks of evening dosing, subjects will begin to take their study medication in the morning (AM) and continue with this dosing regimen throughout the remainder of the study. After 6 weeks of treatment, all subjects initially randomized to 60 mg of GW679769 will be titrated to the higher dose of 120 mg of GW679769 and remain on this treatment for an additional 6 weeks. Subjects randomized to placebo will remain on placebo for the entire 12 weeks of treatment. Safety and tolerability of the assigned treatment will also be assessed. All subjects will participate in the population PK analysis where a total of 6 samples per subject will be taken for analysis during the course of the study. Approximately 1 week after completion of the Treatment Period, subjects will return for a follow-up visit.

**Progress:** The study sponsor terminated MAMC as a study site 24 April 2006, with no patients enrolled. The screening of MAMC patients was planned for July 2006, and the study was expected to close to enrollment at that time.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 204116	<b>Status:</b> Completed
<b>Title:</b> Phase 2, Multi-Center, Randomized, Double-blind, Placebo-Controlled, 3 Arm, 12-Month Study to Evaluate the Effects of GPI 1485 on Erectile Function in Patients Undergoing Bilateral Nerve-Sparing Radical Retropubic Prostatectomy for Prostatic Carcinoma, Protocol Number 0501-0202			
<b>Principal Investigator:</b> MAJ Keith J. O'Reilly, MC			
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Andrew C. Peterson, MC; MAJ Karen C. Baker, MC; COL Robert C. Allen, MC; CPT Brian J. DeCastro, MC; CPT Jack R. Walter, MC; Tammie Bousquet-Cordes, LPN			
<b>Start - Completion:</b> 11/5/2004 - Aug 2005	<b>Funding:</b> Guilford Pharmaceuticals Inc. via The Geneva Foundation		<b>Periodic Review:</b> 8/23/2005
<b>Study Objective:</b> Primary objectives: (1) To compare the effect of a 6-month course of GPI 1485 1000 mg QID vs. a 6-month course of placebo on the EF domain of the IIEF questionnaire 6 months post-NSRRP in men 40-59 years of age. (2) To compare the effect of a 6-month course of GPI 1485 400 mg QID vs. a 6-month course of placebo on the EF domain of the IIEF questionnaire 6 months post-NSRRP in men 40-59 years of age. Secondary objectives: (1) To compare the effect of a 6-month course of GPI 1485 1000 mg QID vs. a 6-month course of placebo on the EF domain of the IIEF questionnaire 6 months post-NSRRP in men 60-69 years of age. (2) To compare the effect of a 6-month course of GPI 1485 400 mg QID vs. a 6-month course of placebo on the EF domain of the IIEF questionnaire 6 months post-NSRRP in men 60-69 years of age. (3) To compare in each age group the effect of GPI 1485 vs. placebo on the EF domain of the IIEF questionnaire 3, 9, and 12 months post-NSRRP. (4) To compare in each age group the time to first recovery of EF curve in each of the GPI 1485 treated group vs. the placebo treated group using a score of 26 on the EF domain of the IIEF questionnaire. (5) To compare in each age group the effects of the 2 active GPI 1485 treatment groups on the EF domain of the IIEF questionnaire. (6) To compare in each age group Viagra® use over an 11-month period in the GPI 1485 vs. placebo treated groups. (7) To examine in each age group Health Related Quality of Life (HRQOL) status post-NSRRP using the RAND 12-item Health Survey v2 (SF-12 v2) and the UCLA Prostate Cancer Index Short Form. (8) To evaluate in each age group the safety of GPI 1485. (9) To evaluate in each age group the pharmacokinetics of GPI 1485. (10) To evaluate the efficacy and safety for age-combined GPI 1485 and placebo groups.			
<b>Technical Approach:</b> This trial will be multi-center, randomized, double-blind, placebo-controlled, 3-arm study to evaluate in men 40-59 years of age the effects of GPI 1485, 1000 mg QID and GPI 1485, 400 mg QID on erectile function post-Bilateral Nerve Sparing Retropubic Radical Prostatectomy (NSRRP) after 6 months of treatment. During an additional 6 months of follow-up, the study will evaluate long-term benefits of GPI 1485. Randomization will be stratified by age group (40-59 vs. 60-69 years of age) and by site. Patients will be randomized to one of three study arms in a 1:1:1 ratio. Arm 1: GPI 1485 1000 mg QID for 6 months; Arm 2: GPI 1485 400 mg QID for 6 months; Arm 3: Placebo QID for 6 months. Patients meeting screening criteria and enroll in the study will have a total of 8 protocol specified visits for safety, concomitant medication, and compliance assessments. Six will be office visits: screening visit, baseline visit (Visit 0), surgical period (Visit 1), and visits after approximately 3 (Visit 3), 6 (Visit 4), and 12 (Visit 6) months post-surgery. There will also be two telephone follow-up visits after approximately 1 month (Visit 2) and 9 (Visit 5) months post-surgery. Patients will also have electronic Patient Experience Diary efficacy visits at 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 months post-surgery. Patients will not be required to return to the office or speak to study personnel over the telephone in order to complete the			

electronic PED visits, but will be required to complete protocol specified study questionnaires via an electronic PED. The electronic PED will be used daily to track randomized study medication use until 6 months post-surgery. The electronic PED will be used weekly to track Viagra® use from 1 to 12 months post-surgery.

**Progress:** This protocol closed to enrollment in March 2005, and a site close out visit conducted in May 2006, by phone. Two subjects were randomized, one completed study treatment, and one withdrew consent. No internal serious adverse events were reported.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205073	<b>Status:</b> Ongoing
<b>Title:</b> A Phase 2, Randomized, Multicenter, Placebo-Controlled, Double-Blind Dose-Ranging Clinical Trial to Study the Efficacy and Safety of 5, 15, or 25 mg/day of CyPat™ (Cyproterone Acetate) for the Treatment of Hot Flashes following Surgical or Medical Castration of Prostate Cancer Patients, Protocol #DR-PCA-201		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; ; Dieter Kirchheim, MD; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; CPT Brian J. DeCastro, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 7/26/2005 - Jun 2006	<b>Funding:</b> Duramed via The Geneva Foundation	<b>Periodic Review:</b> 4/25/2006
<b>Study Objective:</b> Primary objectives are to compare the efficacy of 5, 15 and 25 mg/day of CyPat™ to placebo when used as "add-on" therapy in reducing the frequency and average severity of moderate to severe hot flashes; to compare the safety of 5, 15 an 25 mg/day CyPat™ to placebo when used as "add-on" therapy; based on the efficacy and safety of each dose, identify the minimally effective dose to be evaluated in a future Phase 3 study. Secondary objectives are to compare the efficacy of 5, 15 and 25 mg/day of CyPat™ to placebo when used as "add-on" therapy in reducing the average severity of all hot flashes and to compare the efficacy of 5, 15 and 25 mg/day of CyPat™ to placebo when used as "add-on" therapy in elimination of all hot flashes.		
<b>Technical Approach:</b> Randomized, double-blind, placebo-controlled 12-week study to compare the efficacy and safety of 5, 15 and 25 mg/day CyPat™ to placebo when used as "add-on" therapy in addition to a stable course of standard pharmacological therapy for prostate cancer in patients with mild to moderate vasomotor symptoms (hot flashes) following surgical or medical castration. A total of 400 patients will be randomized, 100 per treatment arm to achieve 75 analyzable patients per arm. After consenting on the first day of Screening Period, potential patients will have the following: medical history-including history of hot flashes, physical examination-including assessment of known thromboembolic risk factors, and clinical laboratory evaluations. Once results of the Screening Period evaluations are obtained, those patients thought to be likely to meet the inclusion and none of the exclusion criteria will be invited to participate in a one week single-blind placebo run-in period. Patients must demonstrate at least 21 moderate to severe hot flashes during the 7-day Placebo Run-In Period (this number may be prorated based on the actual duration of the run-in period). Four hundred patients found to meet all the eligibility criteria following the single-blind Placebo Run-In Period will be randomized equally to one of the four double-blind treatment groups: CyPat™ 5, 15 or 25 mg/day or to placebo for a total of 12 weeks. Patients will return for follow-up evaluations each month after beginning double-blind treatment. Patients will maintain a daily paper diary to record the frequency and severity of hot flashes during the treatment period. In addition, a brief physical evaluation will be done, diaries will be reviewed and any adverse events will be recorded at each follow-up evaluation.		
<b>Progress:</b> This protocol remains open to enrollment with one patient who screen failed due to a lack of hot flashes.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205086	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Double Blind, Placebo and Active-Controlled Efficacy and Safety Study of SSR240600C, in Patients with Overactive Bladder or Urge Urinary Incontinence, Protocol # ACT 5190		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Karen C. Baker, MC		
<b>Start - Completion:</b> 9/1/2005 - May 2006	<b>Funding:</b> Sanofi Aventis via The Geneva Foundation	<b>Periodic Review:</b> 8/10/2006

**Study Objective:** Primary objective is to evaluate the effect of SSR240600C versus placebo, on maximum bladder capacity using cystometry in Overactive Bladder (OAB), Urge Urinary Incontinence (UI) patients. Secondary objectives will be to assess the effect of SSR240600C on: (1) Additional cystometric endpoints including: maximum detrusor pressure, volume at first desire to void, volume at first unstable contraction. (2) Clinical Endpoints including: micturition frequency, .incontinence episodes, urgency episodes, nocturia (each per 24 hours), and subjective measures including patient's perception of improvement and quality of life measures and (3) Safety and tolerability including adverse event assessment, laboratory and ECG monitoring.

**Technical Approach:** This is a multicenter, prospective, randomized, double blind, and placebo controlled study with calibrator. Patients will be randomly assigned to one of three groups: (1) SSR240600C 500mg/day (2) Tolterodine 4 mg/day, (3) Matching Placebo. Subjects will be selected based on clinical signs and symptoms and urodynamic confirmation consistent with a diagnosis of OAB/UI. Following initial screening and obtaining informed consent, the subject will be instructed on the completion of a voiding diary. If eligible according to the inclusion/exclusion criteria the subject will be randomized to one of the groups noted above and treated for 4 weeks. Cystometrograms (CMG) will be performed at randomization visit prior to study drug intake, and at the completion of four weeks of treatment. In addition to the cystometric endpoints, additional therapeutic efficacy parameters will be recorded through the use of daily voiding diaries, a health related quality of life measure (King's Health Questionnaire) and a subjective assessment of disease state (Visual Analog Scale). The study will consist of a 7-day screening period followed by a four-week treatment period, completing a 7-day follow-up period, for total patient participation duration of approximately 42 days.

**Progress:** A study site close out visit was conducted in August 2006; no subjects were enrolled in this protocol and no outstanding regulatory issues were reported.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205116	<b>Status:</b> Terminated
<b>Title:</b> A Randomized, Double-Blind, Parallel-Design, Placebo Controlled Study to Evaluate the Effects of 5 mg Tadalafil (IC351, LY450190) and 50 mg Sildenafil Administered Once Daily for 6 Months on Visual Function in Healthy Subjects or Subjects with Mild Erectile Dysfunction, Protocol H6D-MC-LVGO		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; COL Robert C. Allen, MC; LTC William R. Raymond IV, MC; LTC Roger K. George, MC; COL Elizabeth A. Hansen, MC; COL Robert A. Mazzoli, MC; LTC Darryl J. Ainbinder, MC; COL Craig D. Hartranft, MC; LTC Mark L. Nelson, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 11/4/2005 - Jul 2006	<b>Funding:</b> Lilly ICOS LLC via The Geneva Foundation	<b>Periodic Review:</b> 8/10/2006

**Study Objective:** The primary objective of the trial is to evaluate mean changes from baseline to endpoint in dark-adapted bright flash b-wave amplitude on ERG in healthy subjects or subjects with mild ED receiving daily administration of 5 mg tadalafil compared to subjects receiving placebo for 6 months. Secondary objectives (1) the effects of daily administration of 5 mg tadalafil compared with placebo after 3 and 6 months, (2) the effects of daily administration of 50 mg sildenafil compared with placebo after 3 and 6 months, (3) the reversibility of any visual effects (should they be observed) 4 to 6 weeks after 6 months of daily dosing.

**Technical Approach:** This is a multicenter, randomized, double-blind, placebo-controlled, parallel-design study to evaluate the effects on vision of daily dosing of 5 mg Tadalafil or 50 mg Sildenafil compared with placebo. Approximately 198 subjects (approximately 66 subjects per treatment group) will be randomized in this study. Stratified randomization will be used to ensure a 1:1:1 ratio of 5 mg tadalafil to 50 mg sildenafil to placebo with regard to the following factors: Base OU (both eyes) average dark-adapted bright flash b-wave amplitude (<400 V, >400 V), investigator site, and subject age (<50, >50 years).

The study consists of 3 periods, Screening Period, Daily Treatment Period, and a Washout Period: During the one month screening period (Visits 1-2), subjects will be consented and evaluated to see if they meet the inclusion and exclusion criterion and then undergo the first of two ophthalmology exams, which will consist of visual acuity testing with refraction, intraocular pressure measurement, Farnsworth-Munsell (FM100) hue test, peripheral vision measurement, retinal inspection, anterior chamber inspection, and lens/cataract grading. These screening tests will serve as baseline measurements for statistical analyses.

The Daily treatment period will last approximately 6 months (Visit 3-5). At visit 3, the subject will undergo ERG testing, which will serve as a baseline ERG for statistical analyses. If subjects do not exhibit any ERG parameters outside the age-adjusted normative range for that study site, they are eligible for randomization and will receive study drug and be instructed to take one capsule daily beginning the following day. On the days of visits 4 and 5, subjects will omit their dose of study drug for those days and report to the research site with the package of study drug dispensed at the previous visit. The subject will receive a dose of study drug from the returned package and then undergo a complete ophthalmology exam. This exam will be timed so that the ERG testing approximately coincides with peak plasma levels for the drugs Tadalafil and Sildenafil. Should abnormalities on visual testing be observed at visit 4, the PI may bring the subject back for further evaluation and retesting within approximately 2 weeks.

After visit 5, subjects will discontinue study drug, enter a 4-6 week washout period and return for Visit 6 (post -treatment follow-up). At visit 6, subjects will undergo a completed ophthalmology exam. Subjects will not receive a dose of study drug at this time. The purpose of this post-treatment follow-up is to evaluate the reversibility of any abnormality identified during testing at visits 4 or 5. The study is complete after visit 6.

**Progress:** This protocol closed to enrollment in February 2006, with no subjects enrolled at MAMC. CIRO terminated this protocol 14 August 2006, due to an unusually long wait for the study sponsor to conduct a site close out visit.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205027	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Toremifene Citrate for the Prevention of Prostate Cancer in Men with High Grade Prostatic Intraepithelial Neoplasia (PIN)		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; ; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; Dieter Kirchheim, MD; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 3/22/2005 - Feb 2007	<b>Funding:</b> GTx, Inc. via Geneva	<b>Periodic Review:</b> 12/13/2005

**Study Objective:** The primary objective of this study is to assess the efficacy of toremifene in the prevention of prostate cancer in men with high grade prostatic intraepithelial neoplasia (PIN). The Secondary objectives of this study are: (1) To assess the safety of toremifene in men with high grade PIN, (2) To assess the effect of toremifene in high grade PIN, (3) To assess the effect of toremifene on lipid levels, (4) To assess the effect of toremifene on hormone levels, (5) To assess the effect of toremifene on total and % free serum PSA levels, (6) To assess the effect of toremifene on AUA symptom score.

**Technical Approach:** There will be two treatment groups included in this trial. One treatment group will receive tablets containing 20 mg toremifene to be taken daily. The other treatment group will receive matching placebo tablets to be taken daily. Each subject randomized into this study will receive up to 36 months of treatment with a tablet containing 20 mg toremifene or matching placebo tablets. The Screening evaluation includes procedures that are necessary to determine subject eligibility for study treatment. The baseline evaluation is defined as an assessment of subject status prior to any study treatment. If the subject is randomized into this study, the results obtained during the screening and/or randomization visits may be used for the baseline evaluation and comparison with results obtained during or at the completion of the study. Patients will have a 3, 6, 12, 18, 24, 30, and 36 month visits. The primary endpoint will be the diagnosis of prostate cancer through prostate biopsy at 12, 24 or 37 months.

**Progress:** This protocol closed to enrollment with eight patients screened at MAMC. Three patients are actively enrolled and remain on study treatment. Three screen-failed and two patients withdrew consent.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06		<b>Number:</b> 203042	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study of the Efficacy and Safety of Dutasteride 0.5 mg Administered Orally Once Daily for Four Years to Reduce the Risk of Biopsy-Detectable Prostate Cancer, Protocol Number ARI40006			
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC			
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; ; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC			
<b>Start - Completion:</b> 5/6/2003 - Mar 2007		<b>Funding:</b> GlaxoSmithKline via The Geneva Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** The primary objective of this study is to assess the effect of repeat oral once daily dosing of 0,5mg Dutasteride compared to placebo on the risk of biopsy-detectable carcinoma of the prostate after 2 years and 4 years of treatment.

**Technical Approach:** This is a four-year, international, multicenter, randomized, double-blind, placebo-controlled parallel group study to evaluate the efficacy and safety of oral, once daily dosing 0.5mg of Dutasteride in reducing the risk of biopsy detectable prostate cancer in men with suspicious PSA and an initial negative prostate biopsy who are thereby at increased risk for developing prostate cancer. Approximately 18 patients will be enrolled here at MAMC. Patients will complete a 4 week placebo run-in followed by randomization to either 0.5 mg Dutasteride or placebo in a 1:1 ratio. For up to 4 years, patients will be given a 6 month supply of study medication to self administer. Patients will return to the clinic every 6 months for assessments and a re-supply of medication until study termination. Patients will be contacted by phone 3 months after each clinic visit and 4 months after the final dose of study medication to assess adverse events and concomitant medications. All patients will undergo a TRUS at 2 years and 4 years.

**Progress:** A total of 16 patients enrolled in this study at MAMC. Seven patients were screen failures and 9 were randomized and remain on study treatment. This study is closed to new enrollment; however, previously enrolled patients will continue in the study for the duration of 2 years.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205135	<b>Status:</b> Ongoing
<b>Title:</b> Acute Urinary Retention and the Role of Fill and Pull Voiding Trials		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Brian J. DeCastro, MC; CPT Jennifer M. Pugliese, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Karen C. Baker, MC; MAJ Mark I. Anderson, MC; CPT Dayne M. Nelson, MC		
<b>Start - Completion:</b> 1/5/2006 - Sep 2007	<b>Funding:</b> DCI	<b>Periodic Review:</b> 8/29/2006

**Study Objective:** Define the role of fill and pull voiding trials versus simple catheter removal in men with acute urinary retention.

**Technical Approach:** This is a prospective randomized study of 100 patients who present to the Urology clinic with acute urinary retention. These patients have or will have a Foley catheter placed to drain their bladder on presentation. Initial evaluation will include urinalysis, urine culture, and routine serum studies. Patients will be started on tamsulosin if not contraindicated or already on alpha-blocker therapy. Those already on alpha-blockers will continue the original therapy. Patients will follow-up with the urology service for catheter removal on day 5-7. Patients will have complete history and physical examination and be randomized to fill and pull voiding trial or catheter removal following consent. Fifty patients will be included in each arm of the study. Patients will have a transrectal ultrasound to size prostate at time of catheter removal. If patients pass voiding trial they will have a follow-up visit at 1 month to assess voiding symptoms. If patients fail voiding trial they will continue with catheter drainage for an additional 5-7 days and have the same method of catheter removal. If patients have success they will have the above follow-up. If patients fail the voiding trial for a second time, they will undergo urodynamics and be managed by current standards of care. Data recorded will include; the cause of retention, American Urologic Association symptom and bother score, serum creatinine, prostate serum antigen (PSA), urine analysis and culture results, prostate size, outcome of voiding trial, and 3 month follow up data.

**Progress:** No work was conducted under this protocol in FY06, due to deployment of study staff. A change of PI from CPT DeCastro to MAJ Peterson was approved; enrollment is planned to being in October 2006, with the assistance of the new AI, Dr. Pugliese.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206031	<b>Status:</b> Ongoing
<b>Title:</b> Adult Circumcision: Template vs Standard Sleeve Technique		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Brian J. DeCastro, MC; MAJ Karen C. Baker, MC; MAJ Mark I. Anderson, MC; CPT Jennifer M. Pugliese, MC; CPT Dayne M. Nelson, MC		
<b>Start - Completion:</b> 2/22/2006 - Jan 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 12/12/2006

**Study Objective:** To compare the Adult template circumcision with the standard sleeve technique.

**Technical Approach:** This study is a prospective randomized study comparing the standard sleeve technique (current standard) with the Adult template circumcision technique. Patients will be randomized to two groups containing 50 patients each. An interim analysis will be done at 50 patients. The two groups will be compared by operative times, blood loss, complication rates, and overall patient satisfaction as assessed by the attached patient satisfaction form. Significance will be determined using the (X2) test with a p value of < 0.05 being significant.

**Progress:** This protocol remains open to patient entry, with no subjects enrolled to date.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206117	<b>Status:</b> Ongoing
<b>Title:</b> Comparison of Non-Contrast Abdominal Computed Tomography (CT) to Contrast CT, Intravenous Pyelography (IVP) and Nuclear Renal Scan for Determination of Renal Function: A Retrospective Review		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jennifer L. Gurski, MC		
<b>Start - Completion:</b> 8/15/2006 - Sep 2006	<b>Funding:</b> DCI	<b>Periodic Review:</b> N/A

**Study Objective:** Objective is to establish the ability of non-contrast CT ("stone protocol CT") to determine renal function without the use of intravenous contrast or radio-pharmaceutical (IVP, contrast CT, or nuclear renal scan).

**Technical Approach:** The CHCS database will be reviewed for patients who have undergone non-contrast CT scanning of the abdomen for any diagnosis. Patients who have undergone subsequent functional studies in addition to the non-contrast study will be included in the study. A multivariate analysis will be performed to determine if non-contrast CT scanning can be used to estimate renal function without the use of contrast agents or radio-pharmaceuticals.

**Progress:** This minimal risk protocol received initial approval by the Expedited Review Committee, effective 15 August 2006. Initiation is pending a list of patients from the Department of Radiology.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202122	<b>Status:</b> Ongoing
<b>Title:</b> Followup of Testicular Microlithiasis in an Asymptomatic Population		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Mark I. Anderson, MC; CPT Brian J. DeCastro, MC; CPT Jennifer M. Pugliese, MC; MAJ Leah P. McMann, MC; CPT Frederick L. Stephens II, MC; COL Raymond A. Costabile, MC		
<b>Start - Completion:</b> 12/27/0253 - Dec 2002	<b>Funding:</b> DCI	<b>Periodic Review:</b> 6/8/2006

**Study Objective:** To determine the incidence of testis tumor at two, five, and ten-year follow-up in the 84 men previously identified with testicular microlithiasis in the original study by Peterson et al. entitled The Prevalence Of Testicular Microlithiasis in an Asymptomatic Screening Population.

**Technical Approach:** Patients will be identified through the data collected at ROTC Advance Camp 2000. All patients identified with TM will be contacted by telephone. If they agree to participate, the study investigator will administer a telephonic questionnaire on year 2002, 2005, and 2010.

**Progress:** This protocol remains ongoing for continued follow-up for the possible development of cancer in a high risk group of 63 subjects that enrolled. Subjects have been contacted by phone, e-mail, and mail. One participant has developed testicle cancer since last follow up.



### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204078	<b>Status:</b> Ongoing
<b>Title:</b> Long-Term Open-Label Extension Trial for Subjects Completing the Phase 3 Trial of Fesoterodine (SP584) for the Treatment of Overactive Bladder Syndrome		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; ; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC; MAJ Leah P. McMann, MC		
<b>Start - Completion:</b> 8/24/2004 - Apr 2005	<b>Funding:</b> Schwarz Biosciences via The Geneva Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** Long-term data on safety, satisfaction and maintenance in subjects taking fesoterodine will be obtained. The subject satisfaction and the treatment benefit of fesoterodine will be assessed.

**Technical Approach:** SP739 is the open-label extension of the double-blind phase 3 trial SP584. Subjects completing the 12 week treatment period in SP584 will have the opportunity to participate in this extension trial. Subjects will be treated from the time of enrollment until fesoterodine becomes commercially available, but no longer than 3 years after enrollment. All subjects will receive 8 mg fesoterodine hydrogen fumarate at the start of the trial. Each subject may request a one time dose reduction to 4 mg fesoterodine hydrogen fumarate after the subject has been on 8 mg fesoterodine hydrogen fumarate for at least 1 month, during a scheduled site visit and upon discussion with the investigator. Such subjects will also be permitted to increase back to 8 mg fesoterodine hydrogen fumarate. This decision can only be made during a scheduled site visit and upon discussion with the investigator. This process can be followed on an annual basis. At a maximum, the number of subjects for this trial will be 810. However, since it is likely that not all subjects treated in SP584 will qualify and choose to enter the long-term open-label extension, it is estimated that at least 450 subjects will be enrolled in SP739.

**Progress:** This protocol closed to enrollment with five patients enrolled at MAMC. One patient completed the study, two patients withdrew consent and one patient remained on active study medication during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206102	<b>Status:</b> Ongoing
<b>Title:</b> Phase II, multicentre, randomised, double-blind, placebo-controlled, pilot study to determine proof of efficacy, safety, tolerability and pharmacokinetics of intravesical PSD597 in the symptomatic management of interstitial cystitis/painful bladder syndrome (IC/PBS)		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> CPT Jennifer M. Pugliese, MC		
<b>Start - Completion:</b> 9/13/2006 - Dec 2006	<b>Funding:</b> Geneva via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary Objective: To assess the percentage of patients who respond to PSD597, assessed as "moderately improved" or "markedly improved" measured by a Global Response Assessment (GRA), compared to placebo, at day 15 following a 5-consecutive day course of treatment.

Secondary Objectives: (1) To assess changes in GRA measured by a 7-point scale, (2) to assess changes in bladder pain measured by 10-point Likert scale, (3) to assess changes in frequency measured by a voiding log, (4) to assess changes in urgency measured by 10-point Likert scale, (5) to assess changes in symptoms and problems associated with interstitial cystitis measured by the O'Leary Sant Interstitial Cystitis symptom and problem indexes (6) to assess the safety and tolerability of PSD597 instilled into the bladder and (7) to characterize the pharmacokinetics of single and multiple doses of intravesical PSD597 in a sub-group of patients.

**Technical Approach:** This is a phase II, multicenter, randomized, double-blind, placebo-controlled, parallel group, pilot study to determine proof of efficacy, safety, tolerability and pharmacokinetics of intravesical PSD597 in the symptomatic management of IC/PBS. 100 subjects with a clinical diagnosis of IC/PBS with symptoms persisting for at least three months prior to study entry and including pain of bladder origin will be enrolled into the study. Following consent, subjects will undergo screening procedures in the clinic within 14 days prior to baseline (day 1). At baseline (day 1), all eligible subjects will be randomly allocated (1:1) to treatment with PSD597 or placebo. Double-blind treatment will be given as a daily instillation for five consecutive days (Monday - Friday, days 1 - 5), to be administered in hospital as an outpatient. Following double-blind treatment, all subjects will attend clinic for follow-up evaluations on days 8 and 15. All subjects will then be offered the option of open-label treatment with PSD597 for five further days (Monday - Friday, days 15 - 19) - administered in hospital as an outpatient. All subjects, whether or not they opt to receive open-label treatment, will attend clinic for further final follow-up evaluations on days 22 and 29.

**Progress:** This protocol remains open to patient entry, with no patients enrolled.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204032	<b>Status:</b> Ongoing
<b>Title:</b> Prospective, Observational Registry and Patient Survey of the Management of Men with Symptomatic Benign Prostatic Hyperplasia (BPH): BPH Registry and Patient Survey Protocol #L8890		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC		
<b>Start - Completion:</b> 4/5/2004 - Jan 2005	<b>Funding:</b> Sanofi-Synthelabo, Inc. via The Geneva Foundation	<b>Periodic Review:</b> 1/18/2006

**Study Objective:** The aim of the overall registry is to examine the characteristics, management practices, and patient outcomes, including symptom amelioration and disease progression, while exploring the effects of demographic factors, comorbidities, and concomitant medications, in BPH patients in the United States. Safety outcomes, including AEs (common complaints), will also be examined in this patient population.

**Technical Approach:** This is a prospective, multicenter, observational database to collect data on the characteristics, management practices, and subject outcomes of men presenting to their urologist or primary care practitioner with LUTS associated with BPH. It will be offered to a geographically representative group of US physicians who will enroll BPH subjects that are primarily managed conservatively (i.e. watchful waiting or medical intervention). In contrast to a randomized, controlled trial, there are limited predefined interventions and the exclusion criteria are limited. The physician makes his/her own clinical decisions; thus, data captured and reported provide current practice patterns related to diagnosis, management, and results. The registry may also assist physicians in subject follow-up and certain practice management tasks. The data collected will serve to inform the medical community on optimal care. Recently, alpha testing of the registry study was performed at approximately 20 to 30 sites to determine the feasibility of completing the forms (i.e. the burden on subjects and physicians, and the sensitivity to the wording of the sexual questions) during a single visit. Enrollment was competitive with a total of approximately 200 to 300 subjects enrolled. The alpha-testing protocol has provided valuable information that has been used in the design of this protocol for the full-scale registry. The full scale registry is planned to include about 500 sites with approximately 7500 subjects with an option to increase the number of sites, the number of subjects per site, and the registry duration. The primary eligibility criterion is the diagnosis of LUTS associated with BPH at baseline regardless of whether subjects opt for watchful waiting, treatment with 5-alpha-reductase inhibitors or alpha-blockers, or combined medical therapy. Subjects who opt for invasive therapy as an initial treatment or have had surgery in the past for BPH are not eligible for this study. This registry may require minimal additional procedures or interventions as determined by the treating physician. Subjects will be excluded if they decline participation; have concomitant lower urinary tract disease or carcinoma, including history of carcinoma of the prostate or bladder; or have a history of prostatic surgery, including minimally invasive procedures.

**Progress:** This protocol closed to enrollment, but remains ongoing to follow fifteen subjects enrolled at MAMC.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 204086	<b>Status:</b> Ongoing
<b>Title:</b> Prospective, Open-Label, Non-Comparative, Multi-Center Study to Evaluate the Efficacy and Safety of Ciprofloxacin Extended-Release (Cipro-XR) 1000 mg Tablets Given Once Daily for 7 to 14 Days in the Treatment of Patients 18 Years or Older with Complicated Urinary Tract Infections Caused by Pseudomonas Aeruginosa and Other Common Uropathogens		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL Robert C. Allen, MC; MAJ Keith J. O'Reilly, MC; MAJ Karen C.Baker, MC; CPT Jack R. Walter, MC; CPT Brian J. DeCastro, MC; LTC Benjamin P. Harrison, MC		
<b>Start - Completion:</b> 9/17/2004 - May 2005	<b>Funding:</b> Bayer via The Geneva Foundation	<b>Periodic Review:</b> 6/27/2006

**Study Objective:** To evaluate the safety and efficacy of Cipro XR® 1000 mg PO given once daily for 7-14 days for the treatment of patients with complicated urinary tract infections caused by Pseudomonas aeruginosa and other urinary pathogens. The primary efficacy parameter will be bacteriologic outcome at the Test-of-Cure (Day +5 to +9 post-treatment) visit. Secondarily, clinical response will be assessed at the Test-of-Cure (Day +5 to +9 post-treatment) visit. Clinical cure will be correlated with bacterial eradication in the patient population valid for efficacy. The rate of relapse between the Test-of-Cure visit and the late post-treatment (Day +28 to +42) visit will be determined for patients with complicated UTI caused by P. aeruginosa. The safety of the drug treatment will be monitored. To enroll a minimum of 8 patients with complicated UTI caused by P. aeruginosa that is clinically and microbiologically valid.

**Technical Approach:** This is a prospective, open-label, multi-center, Phase IV clinical study to evaluate the efficacy and safety of Cipro XR® 1000 mg PO once daily for 7-14 days for the treatment of patients with complicated UTIs. Patients with clinical signs and symptoms of a complicated UTI that meet all other entry criteria will be treated with Cipro XR® 100 mg PO once daily for a planned treatment course of 7-14 days. Types of diagnoses most likely to be infected with P. Aeruginosa at the time of a complicated UTI include: spinal cord injury/trauma, indwelling urinary catheters (including transurethral and suprapubic), quadriplegia or paraplegia, multiple sclerosis, other risk factors for complicated urinary tract infection and a previous history of a UTI or asymptomatic bacteriuria with P. aeruginosa that was susceptible to flouroquinolones. Patient screening will be performed within 48 hours prior to onset of therapy. During the 7 to 14 day treatment period, there will be an office visit on Day 3-5 of therapy to assess clinical progress. After completion of treatment, there will be a Test-of-Cure (Day +5 to +9 post-treatment) visit for all patients, and for all patients with complicated UTI due to P. aeruginosa, a late follow-up (day +28 to +42 post-treatment) visit to determine the rate of relapse. If, following a full course of therapy, the investigator feels that continued antimicrobial drug therapy is warranted, the patient must be classified as a treatment failure. Before required alternative antimicrobial drugs are given, however, the patient must be fully evaluated and appropriate laboratory tests and cultures performed so that the required information will be available in order to evaluate the study drug.

**Progress:** This protocol closed to enrollment with five patients enrolled. Three patients completed the study, one patient screen-failed and one patient withdrew consent due to needing further antibiotic treatment. The protocol remains ongoing pending a final site close out visit by the study sponsor.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203081	<b>Status:</b> Ongoing
<b>Title:</b> Study of the Safety and Effectiveness of the Mentor Two-Piece Inflatable Penile Prosthesis, Protocol Number U108-802-4		
<b>Principal Investigator:</b> MAJ Andrew C. Peterson, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Karen C. Baker, MC; ; MAJ Michael J. Sebesta, MC; CPT Jennifer M. Pugliese, MC; MAJ Keith J. O'Reilly, MC; COL Robert C. Allen, MC		
<b>Start - Completion:</b> 7/10/2003 - Jun 2004	<b>Funding:</b> Mentor via The Geneva Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** To demonstrate safety and effectiveness of Mentor's Two-Piece Inflatable Penile Prosthesis in men who are undergoing surgical treatment of erectile dysfunction.

**Technical Approach:** This protocol is a multi-center trial. The baseline, pre-operative physical and psychological assessment will serve as a control for each subject. Post-operative measurements of penile erection and psychological assessment should provide a demonstration of the efficacy associated with the penile implants. Patients will have the following baseline study procedures within 30 days of surgery: medical history, physical exam, penile history and measure, psychometric testing with patient satisfaction questionnaire (PSQ), investigators assessment of erectile dysfunction. One or more of the following tests may be used to confirm the diagnosis of erectile dysfunction: Doppler arterial flow, dynamic infusion cavernosometry, rigiscan, and snap-gauge. The operative procedure will take place no more than 30 days after the baseline visit and will record penile measurements and the device catalog number and lot number, anesthesia and other procedure related information. There will be 3 post-operative follow-up evaluations conducted 3-6 weeks after implantation, at 6 months, and 12 months. At each of these follow-ups the following evaluations will be conducted: penile rigidity, adverse event evaluation, urinalysis (12 month follow-up only), patient satisfaction questionnaire (6 and 12 month follow-up only), penile rigidity will be adequate if it is sufficient for sexual intercourse, as determined by the Investigator during postoperative exams and by asking the patient about his ability to perform sexual intercourse. Safety assessment will include: incidence on a per subject basis of all complications (e.g. device malfunctions or infection), time to occurrence of all complications. This study will assess the psychological impact on the subject of implantation of the device. The primary hypothesis will be tested by placing an exact two-sided 95% confidence interval on the re-operation rate. If the upper bound on this confidence interval is less than 0.193 than the null hypothesis will be rejected in favor of non-inferiority to Alpha 1.

**Progress:** This study remains open to enrollment, with eleven subjects enrolled who have completed the study.

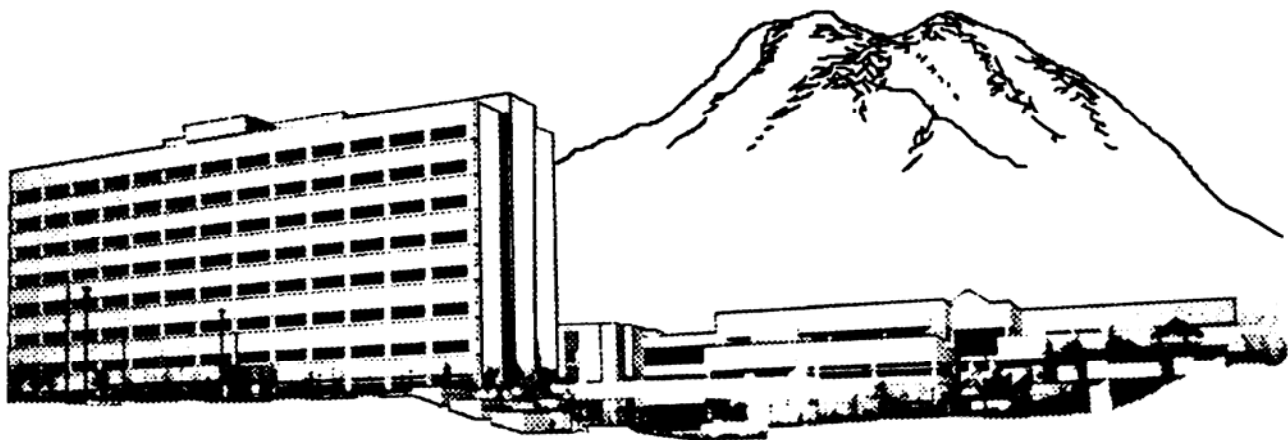
### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205088	<b>Status:</b> Ongoing
<b>Title:</b> The Value of Resistive Index: A Longitudinal Study of Confounding Variables and Their Impact - A Pilot Study		
<b>Principal Investigator:</b> CPT Jennifer M. Pugliese, MC		
<b>Department:</b> Surgery/Urology	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; LTC Benjamin W. Starnes, MC		
<b>Start - Completion:</b> 5/24/2005 - Dec 2008	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/10/2006

**Study Objective:** To determine the course and variability of resistive index as measured by Doppler ultrasound in patients with new onset hypertension over time as their disease progresses and new medications are added.

**Technical Approach:** In this prospective, observational study, a database containing demographic and medical information will be constructed for patients with newly diagnosed hypertension. Candidates for the study will be identified by their primary care providers and referred to the vascular surgery clinic for consideration for the study. A baseline Doppler ultrasound and resistive index calculation will be performed at that point prior to the initiation of any medical therapy for their hypertension. A group of healthy volunteers will also receive a Doppler ultrasound measured resistive index calculation as a control group. Doppler ultrasound and resistive index calculations will then be undertaken at three month intervals in the study patients as well as in the control group. We hope to better determine the utility and accuracy of resistive index in diagnosing renal artery stenosis and determining which patients would benefit from surgical intervention based on the information obtained from this study.

**Progress:** This protocol remains open to enrollment with no subjects enrolled. Recruitment continues.



## Detail Summary Sheets

Vascular Surgery, Department of Surgery

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206012	<b>Status:</b> Ongoing
<b>Title:</b> A Comparative Prospective, Randomized, Double-Masked, Parallel Group, Sham-Controlled Trial of MIST Therapy for the Reduction of Pain in Chronic Lower Extremity Ulcers		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> Mary Anne Landowski, MSN, RN; LTC Benjamin W. Starnes, MC; Monica H. Schweinberger, DPM; Leslie B. Schoneman, PA-C; Gary P. Degen, DPM; Vickie R. Driver, DPM; Thomas S. Roukis, DPM		
<b>Start - Completion:</b> 1/17/2006 - Apr 2006	<b>Funding:</b> Celleration, Inc. via Geneva Foundation	<b>Periodic Review:</b> 10/18/2006

**Study Objective:** Primary Objectives: Effectiveness (1) to assess the reduction in baseline numeric pain rating scale scores comparing MIST Therapy in relation to sham control through treatment week 4. Safety: (2) to compare the incidence of adverse events among patients receiving MIST Therapy in relation to the sham control treatment group. Secondary Objectives: (1) to compare the use of analgesic medication between the two treatment groups through treatment week 4 and (2) to compare the quality of life scores using an SF-12v2 scale between the two treatment groups through treatment week 4.

**Technical Approach:** The trial is designed as a comparative, prospective, randomized, double-masked, parallel group, controlled, multi-center study of patients presenting with chronic non-healing lower extremity venous insufficiency, arterial or sickle cell ulcers. To be eligible for randomization patients must complete a 14 day period of documented, stable, acceptable standard of care under the care of the principal investigator and must demonstrate an average Visual Analogue Scale (VAS) score of  $\geq 4$  (Range 0 - 10), calculated from two VAS evaluations during the last week of the 14 day lead-in phase. No VAS evaluation can be less than 3 and the two evaluations cannot be different by more than three to be considered stable and eligible for randomization. Patients will be allowed to take pain medications as needed during the lead-in period and during the study protocol. Patients will also be allowed to use antibiotics during the 14 day lead-in period if deemed clinically necessary by the investigator. Patients will not be allowed into the study while actively using antibiotics but can remain in the study if antibiotics are clinically required later in the course of the trial. A patient who completes the 14 day documented stable standard of care lead-in phase for the index ulcer(s), demonstrates a stable VAS average pain score and who meets all other study inclusion/exclusion criteria will be randomized to receive one of two treatment courses: a) standard of care with MIST Therapy or, b) standard of care with a sham control. All patients will receive three treatments per week for 4 weeks. Patients must receive 9 of the total 12 treatments and cannot miss more than two consecutive treatments to be considered evaluable. Investigators will be allowed to use their own standard dressings as appropriate for the moisture balance of the ulcer but these will only include standard hydrocolloid, hydrogel, alginate or foam dressings. Changes from one type of dressing to another (e.g. alginate to hydrocolloid) will be allowed as deemed necessary for moisture balance. No advanced or impregnated dressings will be allowed during the study. No topical antibiotics or antibiotic dressings (silver, iodine, etc) will be allowed. Following randomization, ulcer assessments, VAS pain scales and adverse event assessment will be conducted at weekly intervals through week 4; analgesic assessment will be performed three times per week on treatment days; Quality of Life (QOL) scales will be conducted at baseline, week 2 and week 4; sharp debridement will be performed only once per week if deemed necessary by the investigator.

**Progress:** This protocol remains open to subject entry. No subjects were treated during FY06. Two subjects were screened; one screen failed. The other subject signed informed consent and began the



two-week pre-screening process, but was dropped as the subject did not meet all the eligibility requirements (could not differentiate leg pain from stump pain). Other sites have had similar difficulty enrolling.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203079	<b>Status:</b> Completed
<b>Title:</b> A Double-Blind, Randomized, Parallel Group, Placebo-Controlled Study to Evaluate the Safety and Efficacy of NM-702 in Subjects with Intermittent Claudication, Protocol Number NCI-IC-0201		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Leslie B. Schoneman, PA-C; MAJ Philip S. Mullenix, MC; LTC Benjamin W. Starnes, MC; MAJ Allen D. Rubin, MC; MAJ Tyler L. Seick, MC		
<b>Start - Completion:</b> 9/3/2003 - Jul 2005	<b>Funding:</b> Nissan Chemical Foundation via The Geneva Foundation	<b>Periodic Review:</b> 5/24/2005

**Study Objective:** To determine if 4 mg and/or 8 mg NM-702 BID for 24 weeks significantly improves peak walking time (PWT) when compared to placebo. To determine the safety and tolerability of 4mg and 8 mg NM-702 for 24 weeks through analysis of adverse events, clinical laboratory tests, electrocardiogram and physical examinations. To determine the dose-response profile, specifically, to find out whether the 8 mg dose BID will demonstrate better efficacy (improvement in PWT) than the 4 mg dose BID (e.g. the dose-response trend extends to 8 mg BID level), providing a basis for optimal dose selection.

**Technical Approach:** This is a double-blind, parallel-group, dose-response study in which subjects are randomized to receive either 4 mg or 8 mg of NM-702, or placebo, BID for 24 consecutive weeks. This study will look at males or females 50 years of age and older that have been diagnosed with intermittent claudication. Approximately 25 patients will be enrolled into this study here at MAMC. There will be a Screening Visit, three Baseline Visits at least 3 but no more than 10 days apart, in order to obtain 3 baseline tests on separate days, Treatment Visit 1(also Baseline Visit 3) study drug for weeks 1-6 will be dispensed at this visit, Interim Visit 2 study drug for weeks 7-12 will be dispensed at this visit, Interim Visit 3 study drug for weeks 13-18 will be dispensed at this visit, Interim Visit 4 final study drug for weeks 19-24 will be dispensed at this visit, a Primary Endpoint Assessment Visit 5 for primary safety and efficacy follow-up assessments, Follow-up visit 6.

**Progress:** This protocol reached accrual goals and closed to enrollment in April 2005. A site close out visit was conducted May 2006, with 49 MAMC patients consented/screened, 23 randomized and 21 who completed the entire study period. Three subjects eventually withdrew consent. Twenty internal serious adverse events and 17 external adverse events were reported, but none whose relationship was related to study medication.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206094	<b>Status:</b> Ongoing
<b>Title:</b> A Multi-Center, Double-Blind, Randomized, Parallel, Vehicle-and Standard Care-Controlled, Dose-Ranging Study Assessing the Safety and Efficacy of MRE0094 Gel When Applied Topically for 90 Days to Subjects with Diabetic, Neuropathic, Foot Ulcers		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Monica H. Schweinberger, DPM; LTC Benjamin W. Starnes, MC; Mary Anne Landowski, MSN, RN; Thomas S. Roukis, DPM		
<b>Start - Completion:</b> 8/3/2006 - Dec 2006	<b>Funding:</b> King Pharmaceuticals Research and Development, INC via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To assess the efficacy of 3 concentrations of MRE0094 gel compared to vehicle gel and standard care on complete healing of chronic, diabetic, neuropathic, foot ulcers when applied topically for up to 90 days.

**Technical Approach:** This is a multi-center, double-blind, randomized, parallel, vehicle-controlled, and standard care-controlled dose-ranging study of topically applied MRE0094 in diabetic subjects with chronic, neuropathic foot ulcers. Three concentrations of MRE0094 gel (5 g/g, 50 g/g, and 500 g/g), a vehicle control gel, and a standard care arm using a hydrogel-based product to provide a moist wound environment will be evaluated in a parallel design. About 300 subjects will be randomized in a 1:1:1:1:1 allocation into 5 parallel treatment arms (~60 subjects per treatment arm) to obtain 290 evaluable subjects. Treatment arms will be MRE0094 gel 5 g/g, 50 g/g, and 500 g/g, vehicle gel, and hydrogel (as part of the standard care only arm). Randomization will be stratified based on baseline wound size.

Each subject will complete a 14-day Screening/Standard Care Run-in (SSCR) Period, a Treatment Period of up to 90 days, and a 28-day Posttreatment Period. Subjects who successfully complete all SSCR Period assessments, and who meet all entry criteria will enter the Treatment Period and be randomized to 1 of 3 concentrations of MRE0094 gel, vehicle gel, or hydrogel (as part of the standard care only arm) using a central randomization procedure. MRE0094 gel, vehicle gel, or hydrogel will be applied once daily to the target ulcer for up to 90 days. All wounds will be covered with a saline-moistened gauze pad following each application of study drug. The dressing will be held in place by wrapping it with rolled gauze, and taping gauze to gauze. All subjects will be given comprehensive standard care for diabetic, neuropathic, foot ulcers during the entire study that will include: (1) off-loading the target ulcer using an unaltered Bledsoe Diabetic Conformer Boot plus crutches or wheel chair as needed; NOTE: subjects with Charcot's deformity may use their Charcot Restraint Orthotic Walker in place of the Bledsoe boot, (2) maintaining a moist wound environment; (3) reminding subjects of the importance of proper nutrition and adherence to glycemic control measures instituted by their health care providers; (4) additional sharp debridement if needed; and (5) infection control measures. Following the Treatment Period, subjects will enter the Posttreatment Period. All subjects (with healed or non-healed ulcers) will continue to be given standard care for their target ulcer as described above. Only subjects with non-healed ulcers will apply hydrogel during the Posttreatment Period. Each subject will complete up to 12 clinic visits over the course of the study during which procedures and assessments of safety, efficacy, and protocol compliance will be performed.

**Progress:** Enrollment is pending a site initiation visit that is scheduled for Oct 31, 2006.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205111	<b>Status:</b> Terminated
<b>Title:</b> A Phase 3, Randomized, Double-Blind, Multinational Trial of Intravenous Telavancin Versus Vancomycin for Treatment of Complicated Gram Positive Skin and Skin Structure Infections with a Focus on Patients with Infections Due to Methicillin-resistant Staphylococcus aureus 0018		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; Monica H. Schweinberger, DPM; Gary P. Degen, DPM; Leslie B. Schoneman, PA-C; Mary Anne Landowski, MSN, RN; MAJ Cecily K. Peterson, MC		
<b>Start - Completion:</b> 12/8/2005 - Jan 2006	<b>Funding:</b> Theravance via The Geneva Foundation	<b>Periodic Review:</b> 7/10/2006

**Study Objective:** To compare the efficacy and safety of telavancin to vancomycin in the treatment of adults with complicated Gram positive skin and skin structure infections with an emphasis in patients with infections due to MRSA.

**Technical Approach:** This Phase 3 study is a randomized, double blinded, active-controlled, parallel-group, multi-center, multinational trial. Since the study is designed to enroll primarily patients with infection due to MRSA, vancomycin is the comparator agent. Approximately 750 patients worldwide will be randomized to either telavancin 10mg/kg IV q 24 hours or vancomycin 1 g IV every 12 hours. In order to maintain the blind, dummy infusions will be used. The minimum duration of study therapy will be 7 days and the maximum allowable duration of study therapy will be 14 days for all patients. The duration of study therapy for each patient will be determined by the investigator as clinically indicated and will continue until resolution of signs and symptoms associated with the skin infection, or until improvement to such an extent that no further therapy is deemed necessary, to a maximum of 14 days. Patients will be treated to intravenous therapy throughout and may not be switched to oral therapy. However, when appropriate and necessary to complete study therapy, patients who are initially hospitalized may be discharged and continue to receive intravenous medication as an outpatient.

For patients with polymicrobial infections involving Gram negative and/or anaerobic bacteria in addition to the Gram positive organism for which study medication is used, ONLY aztreonam and /or metronidazole used in accordance with the manufacturer's package insert may be added to study therapy. Investigators are encouraged to administer aztreonam and/or metronidazole in patients with suspected or proven mixed infections.

Surgical management of the infection is permissible and considered standard of care; however, significant surgical intervention, more than routine debridement, following initiation of the study medication on more than 2 occasions during the study will constitute evidence of clinical failure. The primary efficacy end point is the clinical response at the Test of Cure assessment. For the purpose of analysis, assessment of "not cured" at End of Therapy will be carried forward to the Test of Cure.

**Progress:** This protocol closed to enrollment before any subjects could be screened at MAMC. No formal close out visit was required by the study sponsor since the site had never been activated. The protocol terminated during FY06.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 200088	<b>Status:</b> Completed
<b>Title:</b> A Prospective, Randomized Study Comparing the Outcome of Carotid Endarterectomy Using New Generation Dacron or Expanded Polytetrafluoroethylene (e-PTFE) Carotid Patching		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; COL David F. J. Tollefson, MC; LTC Stephen B. Olsen, MC		
<b>Start - Completion:</b> 8/17/2000 - Jun 2002	<b>Funding:</b> Meadox Medicals via The Geneva Foundation	<b>Periodic Review:</b> 4/26/2005
<b>Study Objective:</b> The primary objective of this study is to compare the performance of the newest generation Dacron and e-PTFE patches with respect to: (1) postoperative stroke/thrombosis, (2) recurrent carotid stenosis and (3) intraoperative handling/blood loss.		
<b>Technical Approach:</b> After informed consent, patients will be randomized to patch angioplasty with either a Hemashield Finesse patch or a Gore-Tex Acuseal patch. Surgeons will rank the handling of the patch on an analog scale. Time to cessation of bleeding will be monitored. Patients will have an intraoperative duplex, and follow-up duplex examinations at 3, 6, 9, 12, 18 and 24 months after the operation. Rates for carotid re-stenosis will be determined. Perioperative and late neurologic morbidity will be identified and determined.		
<b>Progress:</b> This protocol was reported as completed in March 2006. Data collection and interim analysis has been conducted on 71 patients that enrolled and completed the study visits. A final report on the results of data analysis remains pending.		

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202086	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Diabetic Foot Ulcers (Protocol VAC2001-08)		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Monica H. Schweinberger, DPM; Vickie R. Driver, DPM; Gary P. Degen, DPM		
<b>Start - Completion:</b> 9/24/2002 - Aug 2005	<b>Funding:</b> KCI USA via The Geneva Foundation	<b>Periodic Review:</b> 5/23/2006

**Study Objective:** The primary objectives are to determine the incidence of complete ulcer closure, accelerated ulcer closure or facilitation of surgical closure, and change in ulcer area. The secondary objectives are to determine the reduction in complications, including amputations, quality of life, and average total cost of care.

**Technical Approach:** This study will be looking at approximately 18 male or female patients, 18 years of age or older that have diabetic foot ulcers > 2cm<sup>2</sup> in area after debridement. Visit #1- Eligible patients will be given a physical exam, a relevant medical and surgical history will be taken, concomitant medications will be listed, and blood drawn for laboratory tests and the patient will be given a Quality of Life Questionnaire to complete. Visit #2, the patient will be randomized and given their first treatment. At subsequent visits the study group patients will have medical and medication histories updated, digital photographs will be taken of the wound, measurements taken, dressing applied and instructions on continued care given. The control group will receive standard of care treatment. All patients will receive off-loading therapy preventatively and therapeutically as indicated. Off-loading therapy is used to keep pressure away from the wound area by means of the use of a special shoe, boot, cane, or, in some cases, a wheelchair. No patient will remain in the study for longer than 12 months (total duration). The wound will be examined for recurrence or determination of ulcer status.

**Progress:** This protocol closed to subject entry in March 2006, with fourteen subjects enrolled, one during FY06. Two subjects withdrew consent, one subject screen failed, two were dropped per the advice of the principal investigator, one was lost to follow-up and nine completed the trial. The role of PI was changed from Vickie Driver, DPM, to Charles Andersen, M.D., in December 2005. The protocol remains ongoing pending study close-out by the sponsor.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 202115	<b>Status:</b> Completed
<b>Title:</b> A Randomized, Controlled Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Amputation Wounds of the Diabetic Foot, Protocol No. VAC2001-07		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Vickie R. Driver, DPM; Gary P. Degen, DPM		
<b>Start - Completion:</b> 12/23/2002 - Sep 2005	<b>Funding:</b> KCI USA via The Geneva Foundation	<b>Periodic Review:</b> 8/24/2005

**Study Objective:** The primary objectives are to determine the incidence of complete wound closure, accelerated wound closure or facilitation of surgical closure, and change in wound area over time. The secondary objectives are to determine the incidence of foot salvage, as defined by retention of transmetatarsal amputation with no further revisions at end of study, incidence of complications, quality of life, and average total cost of care.

**Technical Approach:** This study will be looking at approximately 8-10 male and female patients 18 years of age or older that have amputation wounds of the diabetic foot. Visit #1-Eligible patients will be given a physical exam, a relevant medical and surgical history will be taken, concomitant medications will be listed, and blood drawn for laboratory tests and the patient will be given a Quality of Life Questionnaire to complete. Visit #2, the patient will be randomized and given their first treatment. At subsequent visits the study group patients will have medical and medication histories updated, digital photographs will be taken of the wound, measurements taken, dressing applied and instructions on continued care given. The control group will receive standard of care treatment. All patients will receive off-loading therapy preventatively and therapeutically as indicated. Off-loading therapy is used to keep pressure away from the wound area by means of the use of a special shoe, boot, cane, or, in some cases, a wheelchair. No patient will remain in the study for longer than 12 months (total duration). The wound will be examined for recurrence or determination of ulcer status.

**Progress:** A change of principal investigator was approved in January 2006, from Dr. Driver to Dr. Andersen. This protocol was reported as completed at MAMC in February 2006, with nine subjects enrolled. Six subjects completed the study and one was withdrawn. Two subjects died before study completion; one subject on the control arm died of a seizure and the other died of an MI, but was not on VAC therapy at the time of his death, having been removed from the study two months earlier due to extensive comorbidity.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203055	<b>Status:</b> Ongoing
<b>Title:</b> A Randomized, Controlled, Multicenter Trial of Vacuum Assisted Closure Therapy™ in the Treatment and Blinded Evaluation of Pressure Ulcers, Protocol Number VAC2001-01		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; Mary Anne Landowski, MSN, RN		
<b>Start - Completion:</b> 5/16/2003 - May 2004	<b>Funding:</b> KCI USA via The Geneva Foundation	<b>Periodic Review:</b> 1/24/2006

**Study Objective:** The primary objective of this study is to determine if topical negative pressure therapy delivered by the Vacuum Assisted Closure device is clinically efficacious and cost effective in the treatment of pressure ulcers.

**Technical Approach:** The study will look at 10 males or females, 18 years or older, who have the presence of Stage III or Stage IV pressure ulcers located on the trunk or trochanter region. At Visit 1, the patient will have a relevant medical and surgical history taken; physical exam with height and weight; concomitant medications recorded; blood drawn for lab tests. Visit 2 takes place 7days after visit 1 -debridement and assignment to study or control groups will be done with a 1:1 ratio. Study group will have the V.A.C. therapy; Control group will receive standard of care treatment. Pain assessments are completed; data collected; digital photography; bi-layer tracing of the wound will be measured; Granulation tissue formation will be categorically estimated in % and recorded; wound assessment; Quantitative/Semi-Quantitative Bacterial Cultures performed; Patient will complete the wound pain assessment. The VAS pain assessment will be done 1/2 hour prior and post the wound dressing changes. Visits 3 through 7 (+/- 2 days) and 8 (+/- 7 days) - All patients are placed on appropriate Group II or Group III bed surface; wound examinations and assessments will be done: The same ulcer documentation will be done as in Visit 2 above, plus the Interim dressing changes will be documented, i.e. average number of interim dressing changes calculated per day and per week; a list of materials used are recorded; the occupation of the person performing the dressing changes will be recorded. Visit 9 will be the first long term follow-up assessment of recurrence. Visit 10 will be the second long term follow-up/End of Study visit. No patient will remain on the study longer than 12 months (total study duration). The ulcer will be examined for recurrence or determination of ulcer status and a VAS pain assessment will be completed 1/2 hour before and 1/2 hour after the wound dressing changes.

**Progress:** This protocol remains open to enrollment, with 2 subjects enrolled who completed their portion of the study procedures. One subject dropped out due to lack of efficacy. Investigators anticipate the study sponsor closing this protocol by the first quarter of 2007.



## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205010	<b>Status:</b> Ongoing
<b>Title:</b> Linezolid In The Treatment Of Subjects With Complicated Skin And Soft Tissue Infections Proven To Be Due To Methicillin-Resistant Staphylococcus Aureus		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> Gary P. Degen, DPM; LTC Benjamin W. Starnes, MC; Monica H. Schweinberger, DPM; Vickie R. Driver, DPM		
<b>Start - Completion:</b> 3/3/2005 - Sep 2005	<b>Funding:</b> Pfizer via The Geneva Foundation	<b>Periodic Review:</b> 10/24/2006

**Study Objective:** Primary Objective: To compare the clinical efficacy of linezolid to vancomycin in the treatment of complicated skin and soft tissue infections (cSSTI) due to MRSA in adult subjects at the End of Study (EOS) visit. Secondary Objectives: (1) To compare the clinical efficacy, and safety and tolerability of linezolid to vancomycin in the treatment of cSSTI due to MRSA in adult subjects at the End of Treatment (EOT) visit. (2) To compare the bacteriological efficacy, and safety and tolerability of linezolid to vancomycin in the treatment of cSSTI due to MRSA in adult subjects at the EOT and the EOS visits. (3) To compare the medical resource utilization of linezolid and vancomycin for this subject population.

**Technical Approach:** This is a Phase IV, multicenter, randomized, open-label, trial with two treatment groups, linezolid IV or oral tablets and vancomycin IV infusion, to be administered for a planned duration of 7-14 days of treatment. Subjects with documented MRSA bacteremia may be treated up to 21 days at the discretion of the investigator. Subjects will be randomly assigned to receive either linezolid intravenous (IV) infusion or oral tablets 600 mg every 12 hours or vancomycin intravenous (IV) infusion 15mg/kg per dose every 12 hours in subjects with normal renal function. Dosage and interval should be adjusted based on standard nomograms according to renal function. Vancomycin levels should be performed at the investigator's discretion. Aztreonam intravenous (IV) infusion 1-2 grams every 12 hours may also be administered as required for suspected or proven Gram-negative pathogens until culture results are obtained. If the subject does not have a Gram-negative pathogen, aztreonam will be discontinued, at the discretion of the investigator. An alternative agent may be substituted for aztreonam if the local susceptibility patterns preclude its use or for other reasons the subject may be unable to use it. The agent selected must not have activity against MRSA. Metronidazole intravenous (IV) infusion or oral tablets 500 mg every 8 hours may also be administered as required for suspected or proven anaerobic pathogens until culture results are obtained. If the subject does not have an anaerobic pathogen, metronidazole will be discontinued at the discretion of the investigator. Approximately 600 subjects per arm will need to be enrolled for a total sample size of 1200 subjects. There is no planned formal interim analysis.

**Progress:** This protocol remains open to enrollment with eight subjects enrolled, three during FY06. One subject is deceased (unrelated to study medication) and one subject discontinued. Three subjects had MRSA.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206071	<b>Status:</b> Ongoing
<b>Title:</b> Phase 3, Multicenter, Multi-National, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Alfimeprase in Subjects with Acute Peripheral Artery Occlusion (NAPA-3)		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> LTC Benjamin W. Starnes, MC; MAJ Kelly S. Blair, MC; Leslie B. Schoneman, PA-C; LTC John D. Statler, MC; MAJ Joseph A. Ronsivalle, MC		
<b>Start - Completion:</b> 6/7/2006 - May 2007	<b>Funding:</b> Nuvelo Inc. via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** To evaluate the efficacy of alfimeprase compared with placebo as measured by 30 day open vascular surgery free rate. To evaluate: rate of arterial flow restoration at 4 hours after initiation of study drug, rate of improvement in index limb ankle-brachial index (ABI) by 0.15 at 30 days, change in Walking Impairment Questionnaire functional status scores from baseline at 30 days and safety.

**Technical Approach:** This is a Phase 3, multicenter, multi-national, randomized, double-blind, placebo-controlled trial with the goal of randomizing 300 subjects. Eligible subjects will be randomized in a 1:1 ratio to receive either intra-thrombus alfimeprase 0.3 mg/kg total dose or intra-thrombus placebo. Study drug will be administered as split doses with 2/3 of the total dose given as the first infusion followed in 2 hours by the remaining 1/3 of the total dose as a second infusion. Both infusions will be given as 1 mL/min pulsed boluses. Subjects will receive both infusions unless otherwise indicated. Study drug will be infused and subjects will be clinically monitored and assessed by follow-up arteriogram 4 hours after initiation of the first dose of study drug. Subjects with restoration of arterial blood flow on the 4-hour follow-up arteriogram will receive no further intervention, endovascular therapy for underlying atherosclerotic lesions or open vascular surgery. The decision to proceed to a particular intervention should be based on functional, symptomatic, and/or physical examination criteria along with locally interpreted arteriographic findings. Subjects without restoration of arterial blood flow seen on the 4-hour follow-up arteriogram will only be eligible for open vascular surgery (e.g., thromboembolectomy). Investigators will be instructed to follow the Acute PAO Management Algorithm (Section 3.4.2) that was modified from the recommendations for the Ideal Management Algorithm for the Treatment of Acute Limb Ischemia Due to Acute PAO. Thirty (30) day open vascular surgery free rate will be the primary endpoint. Restoration of arterial flow rate, increase in ABI by 0.15 rate, change in Walking Impairment Questionnaire (WIQ) functional status scores, and safety will be the secondary endpoints. Restoration of arterial flow will be assessed by the investigator and by a blinded, central Arteriogram Review Committee. Length of hospital stay and length of intensive care unit (ICU) stay up to 30 days as well as WIQ scores and increase in ABI by 0.15 rate at 90 and 180 days after study drug infusion will be exploratory efficacy endpoints. Safety will be assessed by monitoring of AEs, SAEs, major bleeding events, ICH, and peripheral arterial embolic events up to 30 days as well as all cause mortality, AEs, surgical and endovascular procedures and amputation at 30, 90, and 180 days.

**Progress:** This protocol is open to patient entry, with no enrollments during FY06. The study sponsor indicates that enrollment in this study is slow. Study staff continues to monitor for eligible subjects.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205091	<b>Status:</b> Ongoing
<b>Title:</b> The Prevalence and Progression of Carotid Artery Stenosis in Patients Undergoing Radiation for Head and Neck Cancer		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Garth S. Herbert, MC; LTC Benjamin W. Starnes, MC; LTC Douglas M. Sorensen, MC; LTC John B. Halligan, MC; CPT Michael J. Wilhelm, MC; Billinda Tatum, RN, CCRC		
<b>Start - Completion:</b> 6/16/2005 - Feb 2015	<b>Funding:</b> DCI	<b>Periodic Review:</b> 5/26/2006

**Study Objective:** (1) To establish the prevalence of carotid artery stenosis and its risk factors in patients with head and neck cancer. (2) To establish the course of progression of carotid artery stenosis in patients undergoing radiation for head and neck cancer. (3) To determine the correlation (if any) of C-reactive protein levels with carotid artery disease in patients undergoing radiation for head and neck cancer.

**Technical Approach:** This is a prospective cohort study. The screening tests are already being offered by the Vascular Surgery Service at MAMC. Eligible patients would be consented and their name, age, social security number, and other demographic data recorded in the ICDB and flagged as a study participant. A short screening questionnaire (recorded in the initial ICDB note) designed to identify other risk factors for or symptoms of carotid artery stenosis will be completed at this time.

Patients referred to the Vascular Surgery Clinic at MAMC would have a screening carotid duplex performed within one month of the initiation of XRT in order to establish the baseline level of disease present in these patients. Each patient will also be asked to complete a questionnaire to determine risk factors for and previous symptoms of vascular disease. The resultant data from each duplex will be recorded in the patient's chart maintained at the vascular surgery clinic, and the questionnaire will be kept in the chart as well. After performance of the carotid ultrasound, the patient will be sent to the lab for blood draw to determine a baseline C-reactive protein level. After radiation therapy, the dose of radiation administered to each carotid artery will be recorded. If a hemodynamically significant stenosis is identified, the patient would be evaluated for a carotid endarterectomy by ACAS and NASCET criteria, as is the standard of care in the Vascular Surgery Clinic at MAMC.

After the initial screening, the patients will undergo follow-up carotid duplexes every six months in order to define the progression of carotid artery disease following radiation therapy. As with the initial duplex, any patient with a hemodynamically significant abnormality on follow up studies would be evaluated for a carotid endarterectomy by ACAS and NASCET criteria. After the screening, positive results requiring further diagnostic evaluation would be compiled and follow-up would be arranged for definitive testing and subsequent risk factor modification and/or intervention. These subjects will be identified as members of the "high risk" subgroup in terms of future stroke potential to their primary care provider. Patients who agree to additional blood draws will also have a C-reactive protein level determined on the same day the follow-up carotid duplex is performed.

**Progress:** This protocol remains open to enrollment with three subjects enrolled who had a carotid duplex performed prior to beginning radiation therapy. Given the small number of patients enrolled thus far, as well as the fact that part of this study is longitudinal in that it will examine

changes in the degree of carotid artery stenosis following radiation, there are no findings or conclusions thus far. All enrolled patients will continue to have screening carotid duplexes and CRP levels drawn approximately every six months.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 203017	<b>Status:</b> Completed
<b>Title:</b> The Prevalence of Three Major Stroke Risk Factors in an Enrolled Medicare Population		
<b>Principal Investigator:</b> COL (Ret) Charles A. Andersen, MD		
<b>Department:</b> Surgery/Vascular Surgery	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> MAJ Philip S. Mullenix, MC; LTC Benjamin W. Starnes, MC; MAJ Rosemary P. Peterson, MC; CPT Garth S. Herbert, MC; CPT Zachary M. Arthurs, MC; CPT Katharine E. Wolcott, MC; CPT Daniel G. Cuadrado, MC; MAJ Allen D. Rubin, MC; Leslie B. Schoneman, PA-C; MAJ Kelly S. Blair, MC		
<b>Start - Completion:</b> 6/18/0282 - Oct 2004	<b>Funding:</b> DCI	<b>Periodic Review:</b> 10/19/2005

**Study Objective:** (1) To establish prevalence of carotid stenosis in an enrolled Medicare population. (2) To establish prevalence of atrial fibrillation in an enrolled medicate population. (3) To establish prevalence of uncontrolled hypertension in an enrolled Medicare population.

**Technical Approach:** As part of a larger hospital-based total cardiovascular healthcare initiative, this study is designed to establish the respective prevalence of significant carotid artery stenosis, atrial fibrillation and hypertension in an enrolled Medicare population of 5000 men and women over the age of 65. This project is designed as the first component of a three-phase stroke screening and risk factor modification study to be performed over several years at MAMC. The first phase will define the prevalence of these three conditions in the target population and establish the participants in this study as tracked entities (each individually flagged as part of a larger cohort) in the hospital's automated integrated clinical database system (ICDB). It is estimated that this screening process will take approximately 36 months.

During the second phase, lasting 36 months per patient from time of initial screening, patients identified to have carotid stenosis, atrial fibrillation or sub-optimally controlled hypertension will have these conditions modified medically and/or surgically in accordance with the current practice guidelines and standards of care in place at MAMC. During this period, the progress of this "high-risk" subgroup will be tracked in the ICDB.

In the final phase, the longitudinal data acquired will be utilized to facilitate critical outcome analysis of the risk-factor modification efforts performed in this high risk subgroup during phase two.

**Progress:** This study has been conducted during the annual Retiree's Health Fair since November 2002, but there was no activity during FY06. Investigators are no longer gathering the type of information generated from this study in this format. The protocol is considered completed. In total, there have been 988 participants.

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206127	<b>Status:</b> Ongoing
<b>Title:</b> A phase 2B long-term, randomized, open-label, safety and tolerability trial comparing [S,S]-Reboxetine (PNU-165442G) with routine care in patients with chronic painful diabetic peripheral neuropathy (DPN) Study Number A6061031		
<b>Principal Investigator:</b> Thomas S. Roukis, DPM		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; Monica H. Schweinburger, DPM		
<b>Start - Completion:</b> 11/17/2006 - Aug 2009	<b>Funding:</b> Pfizer via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** Primary objective is to assess the long-term safety and tolerability of [S,S]-RBX in patients with DPN.

Secondary objectives are to assess the effect of long-term treatment with [S,S]-RBX on neuropathic pain and health-related quality of life in patients with DPN and to assess the effect of long-term treatment with [S,S]-RBX on the use of pain-related medications for the management of DPN.

**Technical Approach:** This is a phase 2B long-term, randomized, open-label, safety and tolerability trial comparing [S,S]-RBX with routine care in patients with DPN. Following the screening visit (V1) is a one-week baseline period. At the end of this baseline period (V2), patients meeting the randomization criteria are randomized to either [S,S]-RBX or routine care in a 1:1 ratio. Approximately 800 patients will be randomized at V2. The maximum trial duration is 2 years, during which there will be 14 clinic visits. Thereafter, a final clinic visit (V15) for follow up, will be undertaken, one week after V14. Patients randomized to [S,S]-RBX will be treated with 1mg Q.D. for the first week after V2. At the end of this week they will return for another visit (V3), where the dose may be left at 1mg or, if required for symptomatic reasons, may be increased to 2mg. Thereafter, if required for symptomatic reasons, stepwise dose increase in 1mg increments, up to a maximum total daily dose of 8 mg, will be possible. For reasons of tolerability, the dose may also be reduced in 1mg decrements to a minimum total daily dose of 1mg. Dose adjustment may occur either at a scheduled clinic visit, or at an unscheduled visit. Following dose adjustment, the patient will be contacted by telephone, within one week, to assess tolerability of the new dose level.

Patients randomized to routine care will receive treatment optimized for them on an individual basis. The investigator will be free to provide whatever pharmacological (other than reboxetine/Edronax or opioids†) or other treatment considered optimal for management of the patient's pain, taking into consideration any side effects associated with this individualized therapy. A centralized interactive voice response system will be employed to manage randomization and the allocation of trial drug treatment. Subject to IRB/EC approval/favorable opinion, this trial will include an additional research component involving collection of biological samples for de-identified genetic analysis. The Clinical Pharmacogenomics Supplement to this protocol provides a description of this additional research. Subjects may participate in this trial even if they choose not to participate in the pharmacogenomics component.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 26 September 2006.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206111	<b>Status:</b> Ongoing
<b>Title:</b> Pivotal Study to Evaluate the Efficacy and Safety of Dermal - Living Skin Replacement (Dermal - LSR) in the Treatment of Chronic Diabetic Foot Ulcers		
<b>Principal Investigator:</b> Thomas S. Roukis, DPM		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; Monica H. Schweinberger, DPM; Mary Anne Landowski, MSN, RN		
<b>Start - Completion:</b> 10/18/2006 - Feb 2007	<b>Funding:</b> ApoPharma Inc. via The Geneva Foundation	<b>Periodic Review:</b> N/A

**Study Objective:** The primary effectiveness objective is to determine the efficacy of Dermal -LSR plus Standard of Care (SOC) for the treatment of chronic diabetic foot ulcers (DFUs) in comparison to treatment with SOC alone. The primary safety objective is to determine the safety of Dermal - LSR plus SOC for the treatment of chronic DFUs in comparison to treatment with SOC alone.

**Technical Approach:** This study will be a pivotal, prospective, randomized, controlled, open-label, multi-center study that will evaluate the effectiveness and safety of topically applied Dermal - LSR in chronic diabetic foot ulcers. The study has an open-label design, with the Investigator and the subject being aware of the treatment group to which a subject is assigned. Subjects will be randomized equally to two groups and receive either four topical applications (one per week for up to 4 weeks) of Dermal - LSR in addition to standard of care or will receive standard of care only. There will be a 2-week screening period. Following the consent process and randomization, subjects will be treated according to assignment. Subjects assigned to Dermal - LSR + standard of care will receive one application weekly for up to 4 weeks (or until the ulcer heals, whichever is sooner). All subjects will receive standard of care for the entire study. If the ulcer heals by week 12 or sooner, subjects will be assessed at 1, 4 and 8 weeks post closure. If ulcer does not heal by week 12, subjects will be assessed weekly and will receive standard of care until week 20. If the ulcer heals between weeks 13 and 19, subjects will be assessed one week post closure and at week 20 for the final study visit. Note that if the ulcer heals at week 19, the one week post closure visit and the final study visit will occur together at week 20. Telephone contact will be made 3 days ( $\pm 1$  day) following each treatment visit (for weeks 1 to 4) to assess the well-being of the subjects. Telephone contact will also be made in weeks 5 and 6. The Biostatistics Group from ApoPharma Inc. will generate the randomization scheme.

**Progress:** This greater than minimal risk protocol received initial approval with stipulations during the convened IRB meeting on 25 July 2006. CIRO approval was obtained 18 October 2006.

## Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 206070	<b>Status:</b> Ongoing
<b>Title:</b> A Two-Part, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Study to Evaluate the Effect of Simvastatin, Losartan, and Pioglitazone on Cardiovascular Disease Biomarkers in Lower Extremity Atherosclerotic Plaque Excised from Patients with Peripheral Arterial Disease		
<b>Principal Investigator:</b> LTC Benjamin W. Starnes, MC		
<b>Department:</b> Surgery/Vascular Surgery		<b>Facility:</b> MAMC
<b>Associate Investigator(s):</b> COL (Ret) Charles A. Andersen, MD; MAJ Kelly S. Blair, MC; Leslie B. Schoneman, PA-C; MAJ Joseph A. Ronsivalle, MC; LTC John D. Statler, MC; CPT Randy J. Kjorstad, MC; CPT Zachary M. Arthurs, MC		
<b>Start - Completion:</b> 6/5/2006 - Jul 2006	<b>Funding:</b> FoxHollow Technologies, Inc. via The Geneva Foundation	<b>Periodic Review:</b> N/A

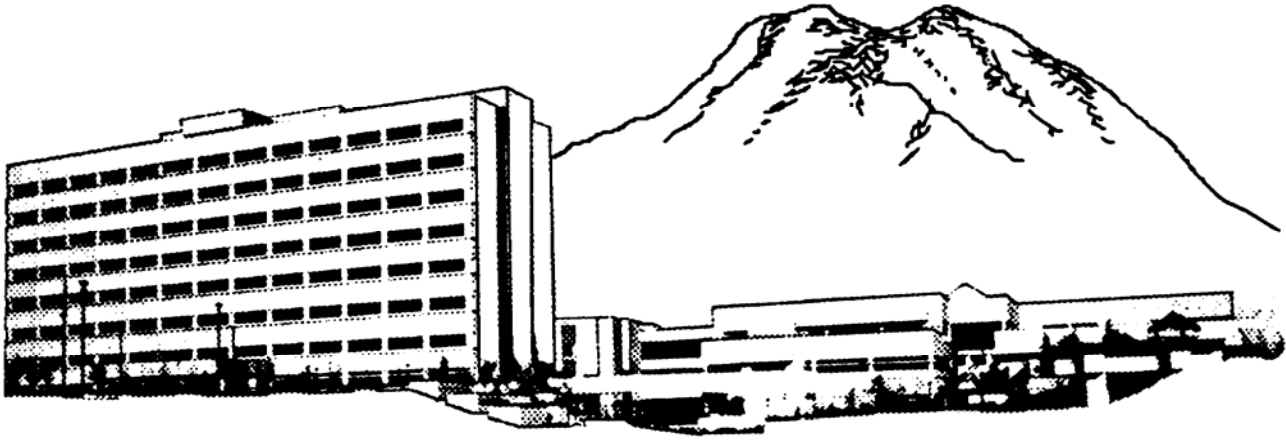
**Study Objective:** To assess the effect of 6 weeks of treatment with simvastatin, losartan or pioglitazone on the RNA expression profile of atherosclerotic plaque excised from peripheral arteries in the lower extremity of patients with PAD. To assess the effect of 6 weeks of treatment with simvastatin, losartan or pioglitazone on protein and lipid biomarkers in atherosclerotic plaque excised from peripheral arteries in the lower extremity of patients with PAD. To correlate plaque protein and lipid biomarker changes following 6 weeks of treatment with simvastatin, losartan or pioglitazone with changes in circulating plasma and/or serum biomarkers and with blood gene expression profiling.

**Technical Approach:** This is multicenter, randomized, double-blind, placebo-controlled, 6-week study, consisting of 3 separate sub-studies in which patients undergoing bilateral lower extremity peripheral artery atherectomy will receive one of three drugs known to have beneficial effect on the risk of cardiovascular disease. Patients will be selected for the particular substudy based on a series of entry criteria and then randomized to the particular agent or placebo for 6 weeks. Following successful completion of a 1 to 2 week placebo run-in period, patients with bilateral symptomatic PAD requiring bilateral revascularization will undergo a unilateral atherectomy using the SilverHawk™ device. The choice of left or right extremity will be determined by random assignment. If treatment of one extremity in advance of the other is indicated either by patient status or physician interest, the investigator will contact the study sponsor to determine whether the patient should be entered. All plaque excised from a given extremity will be collected as part of the study. Based on medical history and concomitant medications, patients will be assigned to one of three treatment groups (simvastatin, losartan, or pioglitazone), and will be randomly allocated to the active drug or matching placebo for a period of 6 weeks. Patients will then undergo repeat peripheral atherectomy on the contralateral leg. A telephone follow-up will be made at Week 8. Blood for gene expression profiling and plasma/serum for circulating biomarkers will be taken at Week 0 and 6. Because of the differential handling of plaque for RNA expression profiling and protein/ lipid measurements, it is not possible to perform both assessments on the same plaque sample. Therefore, the study will be divided into 2 essentially identical parts. In Part A plaque will be evaluated by gene expression profiling. In Part B plaque will be evaluated for protein and lipid biomarkers. An equal number of patients will be enrolled in each Part. After the defined number of patients have been enrolled in Part A for 1 of the 3 study drugs (and its placebo), patients who meet the inclusion and exclusion criteria for that study drug (and its placebo) will then start enrollment in Part B. A total of 336 patients will be enrolled, with a goal of approximately 300 patients completing the study. Each of the treatment groups (simvastatin, losartan, and pioglitazone) will enroll 112 patients, 56 on active drug and 56 on placebo, with the intention of achieving 50 completed patients on active drug and 50 completed patients on placebo. Parts A and



B will each include 28 patients on active drug and 28 patients on placebo, with the intention of 25 completed patients on active and 25 on placebo.

**Progress:** This protocol is open to patient entry, with no patients enrolled during FY06. Active pre-screening for this clinical trial continues.



# **Detail Summary Sheets**

## Weed Army Community Hospital

### Detail Summary Sheet

<b>Date:</b> 30 Sep 06	<b>Number:</b> 205049	<b>Status:</b> Completed
<b>Title:</b> A Phase 2 Study to Evaluate the Reactivity and Tolerability of Intradermally Administered Doses of Coccidioidin in Human Subjects in a Target Population		
<b>Principal Investigator:</b> LTC Gary A. Wheeler, MC		
<b>Department:</b> WACH	<b>Facility:</b> MAMC	
<b>Associate Investigator(s):</b> CPT Karen C. Daily, MC; CPT Arman Faravardeh, MC		
<b>Start - Completion:</b> 8/10/2005 - Jun 2005	<b>Funding:</b> Weed ACH	<b>Periodic Review:</b> 2/22/2006

**Study Objective:** The primary objective of this study of intradermally administered coccidioidin is to determine the prevalence of reactivity to this skin-test antigen in a target population located in a region highly endemic for coccidioidomycosis. The study will also collect safety and tolerability information for the test agent coccidioidin following administration of doses to normal human subjects, as well as the reactivity to the thimerosal preservative in the trace-thimerosal vehicle control.

**Technical Approach:** This is a prevalence and incidence study of coccidioidomycosis conducted in a target population of personnel living in a highly endemic area at Ft. Irwin. 150 volunteers will be tested in a single test period, with the entire study lasting approximately 12 weeks. A single dilution of test agent coccidioidin will be administered along with a vehicle control with trace thimerosal (matching the concentration of the preservative in the coccidioidin). Both test agents will be administered intracutaneously in a double blind fashion, and induration reactions will be measured at 48 hours after injection. Subjects will be evaluated during the test period for adverse events and 5-7 days after the injection for their resolution. All demographic and baseline characteristics of these subjects will be described utilizing summary statistics of mean, standard deviation and median for continuous factors and frequencies for categorical data.

**Progress:** This protocol was completed during FY06, with 120 subjects enrolled; 107 evaluable and 13 lost to follow-up. Subjects were healthy men and women active-duty Soldiers between 18 and 55 years of age who were presumed to be at high exposure risk for coccidioidomycosis because of their training activities in an area endemic for this disease. Each subject received two intradermal injections concurrently and was observed for two hours post-injection. Subjects returned to study site for examination at 48 hours. Follow-up was scheduled at 5-7 days post-injection. Safety: No clinically significant adverse events were seen during the study. Nine of the 107 subjects (71%) who returned for reading of the skin test reaction reported at least one event during the study period. Six reported symptoms judged to be "local, mild", most commonly transient tenderness and pruritis consistent with a positive DTH response. One subject reported lightheadedness that resolved without intervention; this subject did not have a positive DTH response. One subject reporting pruritis was treated with topical steroids. The investigators considered all "local, mild" AE's in the study to be probably related to test agent. Thirteen subjects failed to return for the 48 h reading and those successfully contacted reported no adverse events.

**Activity:** In the study, six subjects were reactive to both the thimerosal-containing vehicle and coccidioidin at 48 hours rendering the coccidioidin data uninterpretable. Nine of 101 (8.9%) subjects reacted with a positive (>5mm) induration response at 48 hours to coccidioidin alone. Excluding one subject (#11) who had lived in Tucson and Texas for 26 years but had only been based at Fort Irwin for ten months prior to the study, the overall reactivity rate was 8.0% (8 of 100 subjects).

**Conclusions:** Coccidioidin was well tolerated under the conditions of the study. Based on the sum

of induration data from the 48 hour interval, evaluable subjects with a positive DTH response to coccidioidin had a mean sum of induration of  $27.22 \pm 7.07$  mm, and a median of 24 mm. Excluding subject #11 yielded a mean of  $27.00 \pm 8.01$  mm and a median of 23 mm.

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